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Technology Review

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CAN TECHNOLOGY SAVE THE ECONOMY?

Yes. But take a deep breath.

p44

The Authority on the Future of Technology
May/June 2009
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ADVANCED MEDICAL TECHNOLOGY THAT

HELPS PEOPLE LEAD RICHER,

FULLER LIVES

NOW.

imagination at work

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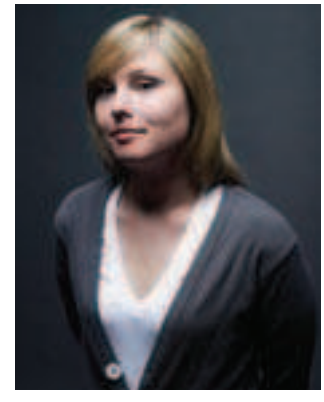

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De Technologia non multum scimus. Scimus autem, quid nobis placeat.

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A LOOK BACK AT THE TR10

Your list of 10 emerging technologies ("TR10," March/April 2009) was interesting, but sometimes implausible as well. Grant me an indulgence and do this one small exercise.

March/April '09

Revisit the technologies you've profiled in previous TR10 issues—say, in 2006 or 2007. I think it would be quite startling to look at how many of those technologies given high praise have died, mutated, or become terminally stuck in an incubation period. How good was *TR* at making the right picks?

The struggle to nurture a good idea from something theoretically possible into a working prototype is child's play compared with the endless real-world demands one must break through to get something produced and into the public arena.

Guy Munsch
Silver Spring, MD

The editors respond:
If we do as Mr. Munsch suggests and look back at our 2006 and 2007 issues, we see that only a few entries (nuclear reprogramming for stem cells, augmented reality for cell phones) have made clear progress. But the TR10 are *emerging* technologies—which, as he says, are unlikely to be overnight successes. It's not surprising, then, that when we examine the first TR10 lists we published, in 2001 and 2003, our performance looks better. Many of those technologies are well on their way to becoming commercial successes, if they haven't already arrived: data mining, biometrics, microphotonics, microfluidics, wireless sensor networks, grid computing, and mechatronic braking systems, to name a few.

BUT WHO'S COUNTING WHAT?

In his article about the difficulty of measuring online audiences ("But Who's Counting?" March/April 2009), Jason Pontin made the case that media companies, and the advertisers they wish to attract, need better tools for measuring how many people are visiting their sites. But while numbers of visitors are important, the most important numbers for advertisers come in the form of dollars, euros, and pesos. What we need is reliable measurement of how much money can be made from sales by advertising on a given media site. The lack of such information has enriched many a media-industry Madoff in my country of Mexico; a standard measure of the impact of advertising online would help prevent this preposterous transfer of money.

José Luis López-Léautaud
Cuajimalpa, Mexico

A NUCLEAR DEBATE

I was heartened to read Andrew Kadak's short piece arguing that nuclear power must be understood as environmentally friendly ("Green Nuclear," March/April 2009). When I managed plutonium manufacturing at the Nuclear Materials and Equipment Corporation (NUMEC) during the late 1960s and early 1970s, we proved that fuel recycling was accomplished easily and that breeder reactors were well suited to that end. We provided fuel for the Fast Breeder Critical Assembly in Japan and for the Zero Power Plutonium Reactor and the Fast Flux Test Facility in this country. Fuel recycling is the way to go!

Bill Frankhouser
Elizabethtown, PA

As a student of nuclear energy at MIT, I am as pro-nuclear as anyone, but I find fault with the assertions of Andrew Kadak and John Gilleland ("Traveling-Wave Reactor," March/April 2009) that we need to develop new breeder reactors to extend the resource base of nuclear power. Fuel composes only 10 percent of the levelized cost of nuclear power, and of that 10 percent, only half is spent on the uranium itself. Furthermore, with uranium at under $130 per kilogram, we have nearly a century's worth of reserves. With minimal exploration, we could easily discover another century's worth at that price; from 2003 to 2005, the world's known reserves doubled thanks to just such an effort.

When will the uranium misers realize that they're solving the wrong problem? Their efforts would be better spent on reducing the capital costs of nuclear power and leaving fuel utilization to another day.

Keith Yost
Somerville, MA

OUT OF THIS WORLD

I read the January/February 2009 issue on my flight home from South by Southwest (the magazine was part of the conference's swag bag). There wasn't a weak story on any page, but one was out of this world: Adam Fisher's oral history of space tourism ("Very Stunning, Very Space, and Very Cool").

While I'll probably never have the millions to afford a flight to the International Space Station, I can rest easy knowing that my $300 three-hour flight in a cramped coach seat was more comfortable than the accommodations afforded professional space travelers. I only wish I had the window seat they had.

Mike Maney
Doylestown, PA

Clarification: The March/April 2009 feature "A Zero-Emissions City in the Desert" does not identify the designer of the Masdar headquarters building. It is the Chicago-based firm Adrian Smith + Gordon Gill Architecture.

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DAVID ROTMAN, who wrote this issue's cover story *("Can Technology Save the Economy?" p. 44)*, interviewed some of the world's leading experts on innovation and economic growth to learn how technology investments in this year's stimulus bill might affect the economy. "Economists generally agree that innovation is in fact the leading factor in creating a wealthy nation," says Rotman. "But I found a huge amount of disagreement on whether the stimulus spending on technology is a great way to help the economy and lay the foundation for future growth or a wrong-headed conflation of fiscal and technology policies. I don't know which position is correct, but I was left with a couple of conclusions. The increase in federal funding for technology and R&D was long overdue. And it is now up to the nation's engineers, scientists, entrepreneurs, and venture capitalists to make sure the money is well spent." Rotman is the editor of *Technology Review*.

DAVID DEAMER has written an essay that is part detective story—recounting his efforts to figure out how life on Earth began—and part thriller: a look at what might be possible if the origins of life were better understood *("First Life and Next Life," p. 66)*. "My research interest is about how cellular life arose on Earth nearly four billion years ago," says Deamer. "I particularly focus on the self-assembly processes that produce protocells, which have some of the properties of life. As a reality check on my laboratory findings, I've traveled to volcanic sites in Russia, Hawaii, Iceland, and northern California, where I test whether the self-assembly processes that are studied in the laboratory can also

work under conditions similar to the prebiotic environment on a hot, early Earth." Deamer, who spent his childhood exploring caves in Kentucky, is a research professor in the Department of Biomolecular Engineering and the Department of Chemistry and Biochemistry at the University of California, Santa Cruz.

MICHAEL ROSENWALD reviews a new procedure that enables remarkably nimble use of a prosthetic by rewiring arm nerves into chest muscles *("A Lifelike Prosthetic Arm," p. 76)*. "Growing up, I always obsessed about my left arm—my throwing arm," says Rosenwald. "I dreamed that that arm would lead to a career as a major-league baseball player. I iced my arm. Used Bengay. Heating pads. I wore a jacket to keep it warm even in the summer. But I never became a major-leaguer and pretty much stopped thinking about my arm until I learned about Todd Kuiken's research. When I saw video of amputees using their prostheses to cook dinner or just put on a belt, I was tremendously moved, and I felt lucky to have two working arms, even if they couldn't get me a pro-baseball career. It was also an example of the kind of technology I find most fascinating to write about: leaps of ingenuity or discoveries that change lives dramatically." Rosenwald, who is based in Washington, DC, has written about the world's most famous bird-flu hunter, a psychiatrist who believes that cats cause schizophrenia, and a doctor trying to regrow body parts with pig bladders. His work has appeared in *Esquire*, the *New Yorker*, *Popular Science*, and *Smithsonian*. He is a staff writer at the *Washington Post*.

GÉRARD DUBOIS illustrated a feature by Emily Singer, *TR*'s senior editor for biomedicine, on how a pill could dim the emotional distress of our worst memories *("Manipulating Memory," p. 54)*. DuBois, who lives in Montreal, is working on two books of illustration, preparing for an exhibition in Paris, and illustrating a regular column in *Time* magazine. He has received numerous awards for his work, including two gold medals from the Society of Illustrators.

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A Manifesto

NEWSPAPERS AND MAGAZINES WON'T VANISH. BUT THEY WILL CHANGE.

Even 15 years ago, Joseph Addison and Sir Richard Steele, those 18th-century London gallants and the founders of the *Spectator*, would have recognized the modes of business that characterized our newspapers and magazines. Not now.

For 300 years, two related sources of revenues sustained journals: subscriptions and advertising. But the Internet taught readers they might read stories whenever they liked without charge, and it offered companies more-efficient ways to advertise. Both parties spent less. Today, media companies are sickly.

As I write, the New York Times Company is threatening to close the *Boston Globe* if the latter will not produce $20 million in union concessions. But those cuts could not make the paper profitable. The *Globe*, which the Times Company bought for $1.1 billion in 1993, would lose $85 million in 2009 without the concessions. Everywhere, newspapers and magazines are going broke.

What can be done to save them? Among those who write about new media, a fashionable wisdom has emerged, expressed most energetically by Clay Shirky, a professor at New York University. In "Newspapers and Thinking the Unthinkable," a much-distributed post on his blog, he writes, "Round and round [it] goes, with the people committed to saving newspapers demanding to know 'If the old model is broken, what will work in its place?' To which the answer is: Nothing. Nothing will work."

The *Götterdämmerung*-of-mainstream-media argument has a weak and strong formulation. Shirky himself is an eloquent exponent of the gentler version. He argues, "Society doesn't need newspapers. What we need is journalism." Shirky believes that the coming decades will see a variety of nonprofit experiments whose funding sources will be similar to those that have sustained *him* as an academic, such as endowments, sponsorships, and grants. One day, some innovator will stumble upon something that will reliably subsidize the journals of the future.

The strong version is most associated with Dave Winer, a grumpy California software programmer best known for helping to develop the Web-feed format RSS and for his blog, Scripting News. Winer has written, and not without glee, "Fifteen years ago I was unhappy with the way journalism was practiced in the tech industry, so I took matters into my own hands. And then dozens of people did, and then hundreds followed, and now we get much better information about tech. It will happen everywhere, in politics, education, the military, health, science, you name it. The sources will fill in where we used to need journalists. ... Everyone is now a journalist."

If media companies can't earn money, and everyone is a journalist, it follows that "amateurs" (Shirky) and "sources" (Winer) will be part of a "decentralized" media (Winer), whose stories will be distributed by "excitable 14-year-olds" (Shirky).

This is all folly and ignorance. Shirky, Winer, and other evangelists know nothing about the business of media. True, the journalists who write about these matters for mainstream media often know as little; I didn't understand much until I became the publisher of *Technology Review*. But Shirky and Winer are disgruntled consumers and, as bloggers, advocates for an insurrection. Thus, they are to be read skeptically. Their prescriptions would be more convincing if they were less polemical and better informed by some knowledge of what publishers sell.

Shirky and Winer share the conviction that media-as-a-business, with its attendant professional writers, editors, art directors, directors of consumer marketing, and advertising salespeople, is dying. That's because they conflate mainstream media with printing presses. As Shirky explains, "Printing presses are terrifically expensive to set up and to run. ... [But] the competition-deflecting effects of printing cost got destroyed by the internet, where everyone pays for the infrastructure, and then everyone gets to use it."

For decades, most print publications have cheaply rented presses owned by third parties—but let that go. The printing press stands here as an objective correlative for the material production and distribution of media. Shirky and Winer's real error is that the physical is the *least* of it. The creation of good journalism is a tremendously laborious process, requiring an infrastructure more expensive than any press. The illustration and design of stories has an infrastructure, too. Developing an audience that will attract particular advertisers requires another infrastructure. Selling advertising requires yet another. These structures, which allow publications to reach large, coherent audiences, can exist only within complex organizations, mostly businesses.

Some of those structures must be reinvented for the Internet. Others, particularly editorial, still work well. I am sure of this, because the number of people who read newspapers and magazines is *growing*. Of course, with few exceptions that growth is all digital. To take one example, between 14 million and 22 mil-

MARK OSTOW

lion read nytimes.com every month; the print circulation of the weekday *Times* is just one million. On any day, 32 million Americans read their news online. Those numbers suggest contented customers. *Of course* there is a good business for mainstream media in electronic publishing. The absorbing question is how to pay for what pleases so many.

It is a canard that neither mainstream media's managers nor its journalists have good answers to that question. There are plenty of stupid publishers and editors, and their publications *will* die; but there are many smart, technology-savvy leaders, too, and *their* publications will prosper. While the details are still debated, the broad outlines of tomorrow's media are becoming clearer. Consumers must pay for more of what they read; publishers and the media buyers who purchase advertising must be given technologies that will make online display ads more competitive with the keyword ads that search firms sell. It won't be easy. I have my own prescription, and those who care (the specifics are technical, and mainly of interest to media professionals) can read my suggestions at www.technologyreview.com/blog/pontin/.

Things change or die, including once-cherished organizations. Today's newspapers and magazines will be transformed or replaced by other publications, which will have new modes of business. A great and terrible clearing is coming. Millions of amateurs will flourish to delight readers. But anyone who tells you that media-as-a-business is dying is wrong.

Write and tell me what you think at jason.pontin@technologyreview.com.

–Jason Pontin

NOTEBOOKS
Expert opinion

ECONOMICS

Stimulating Green Energy

JOSEPH ROMM OUTLINES HOW RENEWABLE-ENERGY TECHNOLOGIES WILL HELP THE ECONOMY.

Can we stimulate the economy and create a sound green-energy policy at the same time? Of course. In fact, it's not possible to have a sustained economic recovery that isn't green.

Our entire economic system is unsustainable. It's a global Ponzi scheme: investors (i.e., current generations) are paying themselves (i.e., you and me) by taking from future generations. To perpetuate the high returns that the rich countries in particular have been achieving in recent decades, we have been taking an ever greater amount of nonrenewable energy resources, especially hydrocarbons; natural capital such as fresh water, arable land, forests, and fisheries; and the most important nonrenewable natural capital of all: a livable climate.

Like all Ponzi schemes, this one will collapse soon—if we don't voluntarily and aggressively switch to an economy built on renewable resources and a commitment to sustaining natural capital. Since action on global warming is inevitable, countries that lead the way in promoting clean technology with incentives and strong, innovation-promoting regulations will gain a competitive advantage. As President Obama said in March, "We can remain the world's leading importer of foreign oil, or we can become the world's leading exporter of renewable energy. We can allow climate change to wreak unnatural havoc, or we can create jobs preventing its worst effects."

The stimulus plan and the president's budget promote energy efficiency, renewable energy, and alternative-fuel vehicles, especially plug-in hybrids—all of which are key to getting us on the sustainable path *(see "Can Technology Save the Economy?" p. 44)*.

States have been showing the way. Half of them have standards that require utilities to purchase certain amounts of renewable electricity. The result: in 2008 U.S. wind energy grew by a record 8,300 megawatts, restoring this country to leadership in that power source. Wind was responsible for 42 percent of all new U.S. generating capacity installed last year.

In the future there won't be a debate about green versus non-green jobs. The only jobs will be ones that don't consume nonrenewable resources and do help avert catastrophic global warming.

Can we stimulate the economy and create a sound green-energy policy at the same time? That, as the president has said, is the only strategy for attaining lasting prosperity. TR

JOSEPH ROMM IS A SENIOR FELLOW AT THE CENTER FOR AMERICAN PROGRESS AND EDITOR OF CLIMATEPROGRESS.ORG.

NETWORKING

Internet Arms Race

WHETHER THE INTERNET WILL HELP OR HINDER THE SPREAD OF DEMOCRACY IS STILL UNCERTAIN, EXPLAINS JOHN PALFREY.

No matter where we are in the world, we change the dynamics of power when we use the Internet for political ends. Take a familiar case: the way community organizers used new technologies in Barack Obama's 2008 election bid, which helped his cause and established a benchmark for other campaigns. In Kenya, the fact that bloggers are reporting publicly on debates in parliament for all the world to see gives politicians reason for pause before they speak and take action. In Switzerland and other advanced democracies, new technologies establish an important space for experimentation in public decision making. Each of these is a good thing.

BOB LONDON

We know, too, that the Internet is used as effectively by states as it is by activists, though often not in the interest of democratization. The Turkish government alters the political discourse when its censors tell the country's Internet service providers to block all access to YouTube—which is widely popular there, as it is in the United States—because a video critical of Atatürk, the country's

modern founding father, popped up somewhere on the site.

The power of the Net is not lost on dictators or military juntas. The Internet is an extraordinary way to snoop on conversations and to look at documents sitting on hard drives in virtually every connected state in the world—as the recent exposure of a vast online spy network, centered in China, made plain.

It is not altogether clear, from the data we have, whether the Internet is a boon to the spread of democracy or its bane. The answer depends greatly on whether you are asking the question from an advanced democracy, from a state in transition, or from a country firmly under authoritarian control.

From the perch of a stable, prosperous state, the Internet is mostly a constructive force. True, we have hard problems to tackle, like how much surveillance we are willing to live with in the name of law enforcement and national security. And we ought to focus on ensuring that our kids, growing up in a digital era, are encouraged to use the Internet in safe, creative ways. But by and large, the Internet provides opportunities to improve our democracies and our economies.

In less democratic societies, sophisticated use of the Internet is limited to the few and the elite. Too often, using these tools puts activists at risk of greater control by the state, through surveillance, censorship, and imprisonment. Political leaders in dozens of states around the world are using digital tools to extend the reach of their power through propaganda, fear, and self-censorship. Resistance is limited to an impassioned, but widely dispersed, community of Internet activists. Bottom-up resistance plainly works at the margins: the tech-savvy can elude most censorship and surveillance most of the time *(see "Dissent Made Safer," p. 60)*. But so too can the smartest of tyrants keep the bulk of their citizens under greater, not lesser, control.

Digital technologies do not have a nature. They are what we make them. For those who care about human rights and the spread of democracy, alarm bells should be going off right now. The Internet may not be the universally positive influence we've been hoping for. TR

JOHN PALFREY IS THE HENRY N. ESS III PROFESSOR OF LAW AT HARVARD LAW SCHOOL AND A FACULTY CODIRECTOR OF THE BERKMAN CENTER FOR INTERNET AND SOCIETY.

MEMORY

Eschew Enhancement

MEMORY-BOOSTING DRUGS SHOULD NOT BE MADE AVAILABLE TO THE GENERAL PUBLIC, SAYS MICHAEL K. AHLIJANIAN.

In an effort to provide Alzheimer's and schizophrenia patients with better, safer medicines, biotech and big pharma have embarked on drug discovery programs targeting multiple cognitive mechanisms. Several of the resulting medications have progressed to late-stage clinical development. For patients suffering from these diseases, the new drugs have the potential to improve cognitive function over a longer term than available treatments, which fade in effectiveness over time.

Given the leaky and lucrative electronic trade in prescription drugs, it's likely that these medicines will be available to healthy people who hope to benefit from them as well.

Who might use them? Students will be tempted, as might players of any game involving counting or remembering (chess, bridge, and even poker and blackjack). Certain professionals might desire a boost in attention or memory: think of interns and residents, or airline pilots. Even the U.S. Department of Defense might be interested in improving the alertness of troops during battle.

But these potentially powerful medicines should not be made available to

everyone, for two reasons. The first is safety. The last several years have provided many examples of side effects, some life-threatening, that emerged only after many thousands of patients had taken a drug (notably the painkiller Vioxx). The risks of harm far outweigh the benefits of modestly augmenting cognitive function in otherwise healthy people.

The second reason is that we still know relatively little about learning and memory and how they are integrated to make judgments and decisions. Drugs used to treat Parkinson's disease, which target a signaling chemical in the brain, have been linked in some cases to gambling and compulsive shopping. Many of those who might consider off-label use of these drugs must use swift judgments to make decisions that significantly affect the lives of others. While new medications might improve certain functions (attention, recall) measured on cognitive tests *(see "Manipulating Memory," p. 54)*, it's unclear what effect this might have on decision making. I am certain that I would not want to be on a plane or in surgery the first time a pilot or surgeon has taken a cognitive enhancer.

Until we have a broad understanding of the safety of these compounds and deeper insight into how they might affect judgment and decision making, the FDA and other regulatory agencies should restrict the drugs to patients under medical supervision. TR

MICHAEL K. AHLIJANIAN IS VICE PRESIDENT OF RESEARCH AT ENVIVO PHARMACEUTICALS.

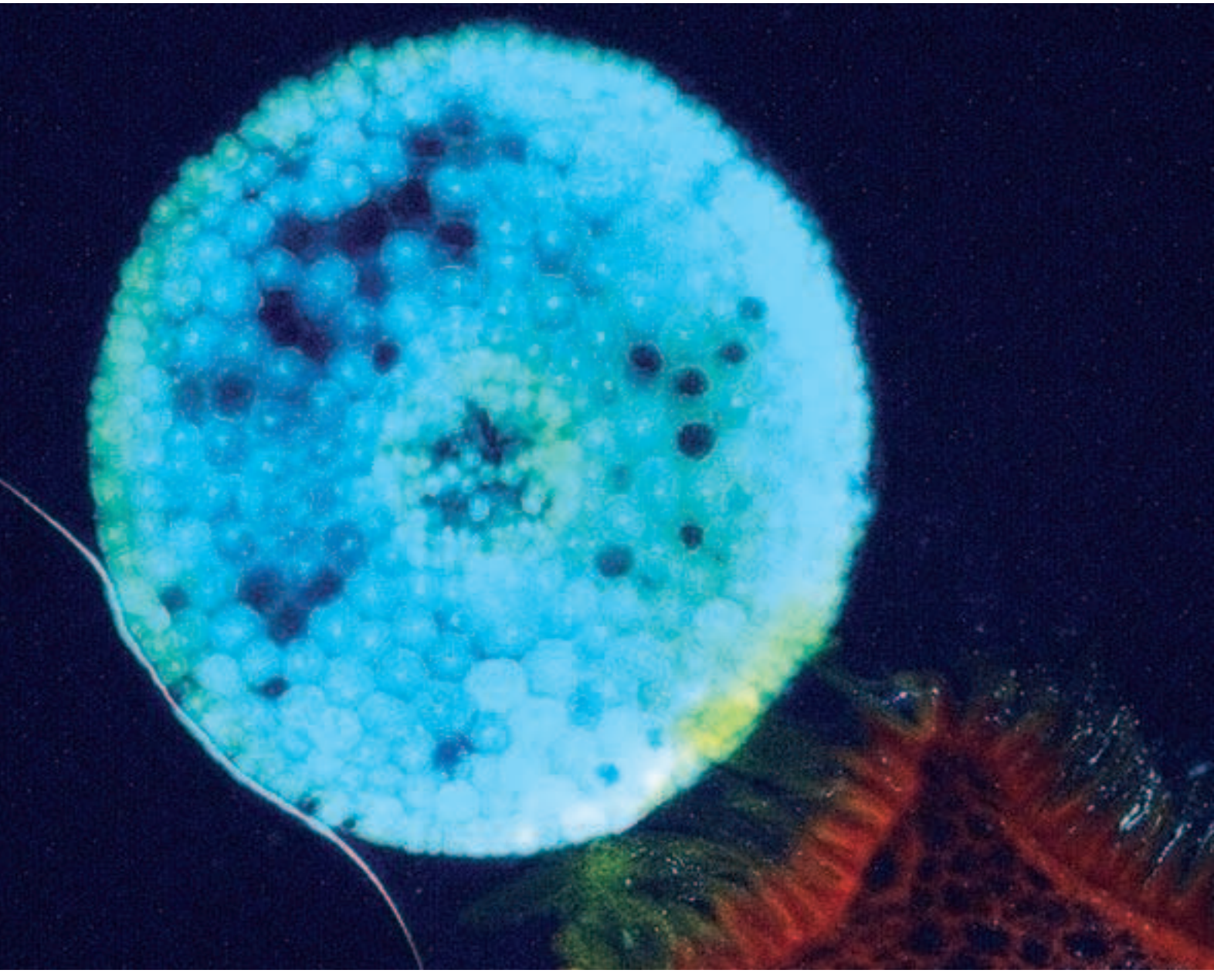
Technology Review
PUBLISHED BY MIT

I am the future of technology.

JOONKI KIM, PHD
FORMER ADVISOR TO THE CEO, SAMSUNG

Dr. Kim's contributions to the IT industry are numerous: he was the visionary behind the Thinkpad tablet computer in 1992; in 1997, he joined Samsung to help its tablet and touch-panel effort; and later, he served as advisor to the CEO. Why does a major contributor to the IT industry turn to Technology Review as a leading source of technology information? "Technology Review is motivating. It's one of my top sources to stay current about new technology information. It's faster in reporting the news compared to any other media property."

Thomas J. Gustainis



BIOTECHNOLOGY IN SPAIN

The biotechnology sector in Spain has grown dramatically, with nearly 700 companies contributing significantly to the Spanish economy.

In a technology park in Tres Cantos, on the outskirts of Madrid, researchers clad head to toe in light-blue protective gear perform experiments with adult stem cells. They're hard at work developing compounds to fight diseases at Genetrix, home to the country's only commercial adult stem-cell facility.

In a nearby lab at PharmaMar's research facilities, a faint tang of salt in the air recalls the sea, as the company investigates applications for its first approved cancer-fighting compound, which is derived from marine organisms.

This region is just one of many around the country in which biotechnology is thriving. According to the Spanish Association of Biotechnology (ASEBIO in Spanish), the sector has flourished in the last five years. By 2007, the latest year for which data is available, the association counted nearly 700 companies engaged in biotechnology, with almost 50 percent growth in funding devoted to research.

PHOTO COURTESY OF ORYZON

Companies in Spain are taking advantage of the country's strength in the life sciences and turning research into useful services and products.

PHOTO COURTESY OF GENETRIX

BIOLOGICALLY ACTIVE

Spain has a long tradition of scientific excellence, particularly in the life sciences. In the past decade the country has focused on transforming its research into consumer-focused companies and products. This advance has come about in large part because of national and local government focus on increasing the country's prominence in biotechnology.

Madrid is home to 75 hospitals, seven of which have more than 1,000 beds, and "the tissue of Madrid health care provides the grounds for clinical trials," according to Jesus Sainz, chair of PromoMadrid. This opportunity for research partnerships, along with more than a dozen universities, top-quality health care, and government stress on biotechnology, has led the region to become a magnet for both local and international companies. Almost half of all new Spanish biotechnology startups locate their head offices in the Madrid region, while pharmaceutical companies, including GlaxoSmithKline, Pfizer, and Bristol-Meyers Squibb, to name a few, have set up research facilities here. The success of the region, says Sainz, is based on the "connection between the universities and research centers and the biotech and pharmaceutical companies."

Two of the most prominent examples of the country's success are PharmaMar and Genetrix, both located on the outskirts of the city.

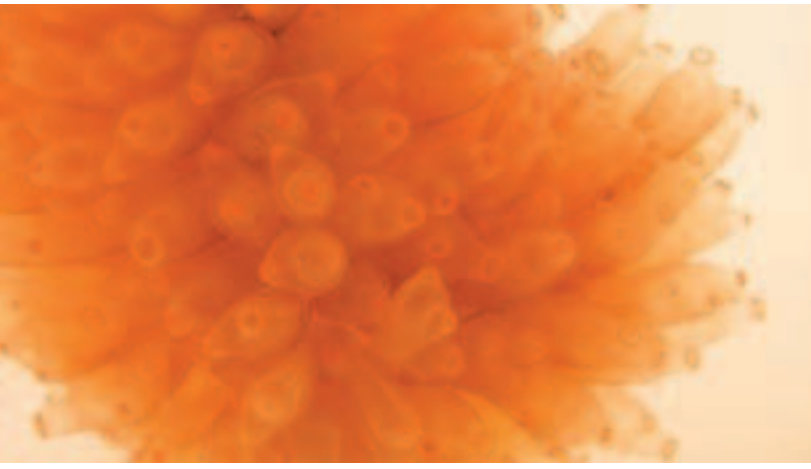
Genetrix, today a family of nine biotechnology companies, was spun off from the National Center for Biotechnology in 2001 by researcher Cristina Garmendia. While Garmendia no longer heads the company, she is a powerful example of the cultural changes in Spain: she is now the head of the newly-created Ministry of Science and Innovation.

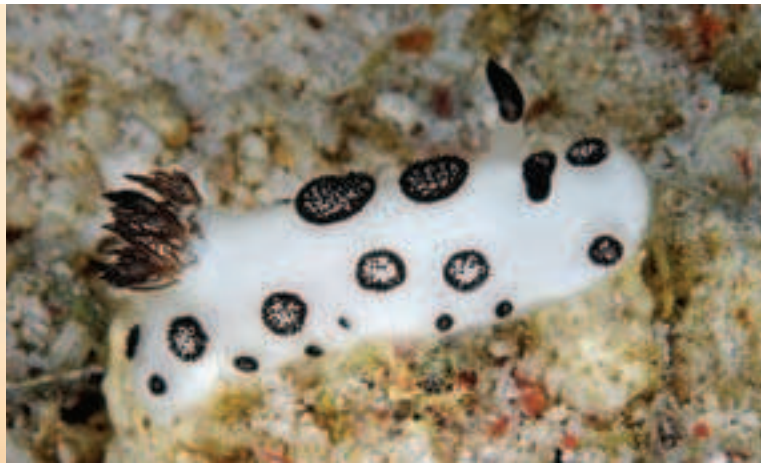
Cellerix, the most prominent Genetrix company, investigates the properties of adult stem cells derived from adipose (fat) tissue. The patient's own fat is removed through liposuction, and its stem cells are isolated and cultivated, then used for the patient's therapeutic needs.

The company is in the final stages of clinical trials of use of these adipose-derived stem cells to treat complex perianal fistulas (abnormal tunnels connecting the rectum with the perianal skin). Today, this inflammatory bowel syndrome is treated only with surgery, which is often unsuccessful and can leave the patient incontinent. In contrast, the stem cell treatment controls inflammation and allows the body to heal and close the fistula. In 2007, Cellerix entered an agreement with Axcan Pharma, a pharmaceutical company dedicated to gastroenterology, for the North American rights to license their product.

Cellerix has a second product in clinical trials, designed to treat individuals who suffer from a rare skin disease called epidermolysis bullosa, in which even minor trauma causes skin loss. The company prepares an artificial skin that is used as an implant and help prevent skin deterioration.

Coretherapix, also within the Genetrix family, is developing products that are based on stem cell therapy for myocardial regen-





Above: PharmaMar has built up the world's largest private library of marine samples to investigate for novel cancer-fighting drugs.

eration after infarctions (heart attacks). Although stem cell therapy to treat heart attack patients has thus far proved elusive, Coretherapix focuses on adult stem cell populations that reside in the heart itself. The company is also developing a growth-factor treatment to stimulate cardiac stem cells to heal the trauma from an attack. Genetrix scientific director Gabriel Márquez sees Coretherapix as the next company to duplicate Cellerix's success.

Genetrix's experience has inspired many others interested in biotechnology, and this has "generated more and more interest in Spanish society," says Márquez. "The number of companies has grown considerably, and the sector has seen a notable increase in support and interest from the government."

PharmaMar, which investigates the antitumor properties of marine life, was created in 1986 by José María Fernández-Sousa. Since then, the company has amassed the largest private library of marine life samples in the world, more than 70,000 to date. Its scientists regularly go on dives in biologically rich areas in cooperation with local governments and research institutions, and they bring back samples of a wealth of underwater life.

These samples are evaluated for cancer-fighting properties. The most successful so far has been Yondelis, PharmaMar's first product to go on the market and the first marine antitumor drug in the world.

"We isolated it from an invertebrate called *Ecteinascidia turbinata*, which was quite difficult," says Luis Mora, general director of PharmaMar. Clinical trials began in 1996, and Yondelis was licensed to Johnson & Johnson in 2001, with shared rights for codevelopment and commercialization. Yondelis has been approved for soft-tissue sarcoma and is awaiting authorization for use against ovarian cancer as well.

Yondelis works by attaching to the tumor's DNA and preventing it from reproducing, halting the tumor's growth. "This mechanism of action is different from other products on the market," says Mora, "and it will work well in combination with other products." With ovarian cancer, he explains, there's a synergistic benefit to the patient when Yondelis is combined with current treatments.

"We think this is only the tip of the iceberg for Yondelis," says Mora.

A second product, isolated from a sea creature called a marine tunicate, is now in clinical trials for use on deep cell lymphomas and multiple myelomas, both cancers for which today there is no effective treatment. Two other products are also in the pipeline, with more on the way.

Noscira, part of the Zeltia Group, in the same family of companies as PharmaMar, takes advantage of the PharmaMar marine library to search for compounds that could treat central nervous system diseases. The company began in 2000 with two patents licensed from the Spanish Research Council; for a family of compounds to treat Alzheimer's and a transgenic mouse that reproduces major features of neurodegenerative diseases. The company has two compounds in clinical trials.

"In the brain of any Alzheimer's patient, you will find tangles and plaques, the two major lesions that constitute hallmarks of the disease," says Belén Sopesén, director of Noscira. "The drugs currently on the market don't work at the level of the lesions, they only treat the symptoms. They don't delay the disease." Noscira's compounds are designed to interfere with the development of the lesions, and thus slow the disease's progression.

In a lab not far from the PharmaMar marine library, Noscira researchers isolate samples of marine compounds in their screening platforms. If one is found to have promise, it's isolated, developed, and tested against disease models. Already they have found a number of marine compounds that have similar mechanisms to combat Alzheimer's, and are preparing them for clinical trials.

Genomica, also a member of the Zeltia group, focuses on microarrays—DNA chips—for sensitive and specific diagnostics. Its most popular product today, sold around the world, tests for the human papilloma virus (HPV). Unlike standard tests, where doctors must interpret the data, their product includes software that gives the doctors the exact results, immediately. It can also detect small amounts of variations of the virus to assist early diagnosis.

PHOTO COURTESY OF PHARMAMAR

After the success of the HPV diagnostic, "We then began considering other diseases caused by viruses or bacteria that could be included" to be addressed by the company's technology, says Rosario Cospedal, CEO, focusing on highly transmissible respiratory diseases and STDs. Genomica also provides DNA identification services for the Spanish police for crime scenes and paternity tests.

SEARCHING FOR DATA

Many researchers who have spent part of their careers in biotechnology with either Genetrix or PharmaMar have moved on to form companies of their own. Juan Carlos del Castillo, formerly with Genetrix, now heads a family of companies called the Bionostra Group. The group's subsidiaries are involved in a variety of aspects of biotechnology; Chimera Pharma, for instance, focuses on virus-like particles that can be used to develop a variety of vaccines and also serve as the basis for therapeutics.

But the product that elicits the most enthusiasm from del Castillo is a recent release from the bioinformatics company Bioalma: he calls it a Google for printed biological data. The engineers at Bioalma have created a system of information retrieval that can search texts and understand the biological meaning of the written word.

"It took seven years of research, and now we have a product that's out in the world and working very, very well," del Castillo says proudly.

Thousands of papers are published every day, and it's nearly impossible for researchers to keep up with the volume. Company engineers needed to develop algorithms for a computer to recognize all the ways of referring to genes, proteins, diseases, symptoms, and other related biological terms, and then create a searchable database of them.

Designing the system proved quite difficult. Says del Castillo, "The challenge for us was to design a computer system capable of reading those papers, understanding what is written, and offering the information to scientists in a structured, comprehensive format." The end result was software called Alma Knowledge Server (AKS). In addition to purchases of AKS by companies such as Roche and Novartis, the National Institutes of Health in the U.S. acquired Bioalma's software to organize its library and facilitate searches for NIH researchers.

But Bioalma engineers realize the importance of allowing all scientists, everywhere around the world, access to an easily searchable database of scientific papers. So they simplified the program from the one that had been purchased by companies and research institutions. In February 2009 they released novoseek.com as a free online tool.

Bioalma alerted the research community around the world, and in novoseek's first month alone, searches from computers around the world, particularly in the U.S., skyrocketed. Scientists can search for "flu" or "influenza," and the system understands both terms and searches through all the papers published. Responses may be filtered by symptoms, by treatments, or by all the genes and proteins that could have a relationship to the flu. In addition to published papers, in March Bioalma added U.S. grants; and by the end of 2009, the system will include patents.

"We think by the end of the year we'll be the world leader for a biomedicine

Return to Spain

Joan Ballesteros had built up a successful biotechnology company called Novasite Pharmaceuticals in San Diego. The company took a known, validated technology—flow cytometry—which evaluates blood samples, and fully automated the system. Suddenly, a machine that could evaluate perhaps some dozens of hand-fed samples a day was transformed into one that could handle thousands, automatically.

Ballesteros saw a wealth of possibilities with the new technology. He imagined how this could aid in the personalization of medicine for leukemia patients: a doctor could put a patient's blood into the machine and check it against thousands of options for fighting leukemia, drugs alone or in combination, in a variety of strengths. And that, to him, was just the beginning.

To make the most out of his ideas, he knew he had to do something that might surprise his research colleagues in the San Diego area, considered one of the world centers of biotechnology. He had to move back home to Spain.

"I turned to my investors and said, 'We should be screening known drugs on patient samples … They told me, 'You will lose our money,'" says Ballesteros. "If I'm wrong, and it doesn't work, they'll lose money. If I'm right, and we're successful, then we'll have so many lawsuits that we'll lose money."

The problem resides with the legal system in the U.S., says Ballesteros, with a culture of easily bringing suits to trial. If a private company were to sign agreements with hospital patients to use their samples for research to help treat diseases, and if that company made money, the patients could sue for a percentage of the profits.

Because of this, biotechnology companies in the U.S. do not work with fresh patient samples; that falls to public institutions such as the National Institutes of Health or public hospitals and universities. "But there have even been cases where the NIH has been sued," says Ballesteros.

In Europe, he explains, if patients have been fully informed and signed consent forms in accordance with all legal and ethical principles (which are essentially the same as In the U.S.), the legal

search system," says del Castillo. They hope to be able to monetize the system through advertisements, as they will regularly reach a broad spectrum of the international scientific community.

COMPUTATIONS FOR THE FUTURE

Search optimization also inspired Ignasi Belda when he and his partners in Barcelona created Intelligent Pharma, "a kind of a Google for compounds," says Belda.

They've developed a computerized system called Helios to search for molecules that might match the functions of ones that researchers plug into the database.

"They connect to our website, they put in the compound that they want to mimic, and then they click 'search'," says Belda. "Our supercomputer does the calculations to obtain a list of the compounds that have the same biological activity as the compound that the user introduced."

To do this, they've created algorithms that calculate the physical and chemical properties of the molecule, in three-dimensional space. "It's a kind of virtual atom that we move around the compound," says Belda. By testing the virtual interactions between the compound and their virtual atom, they generate 22 different fields, such as charge, hydrophobicity, and ability to accept hydrogen bonds. The system runs through millions of compounds in a database to determine which ones might have the same fields, and thus perhaps the same functionality.

"This might be helpful if you have a natural product that's difficult to synthesize and you need another compound more chemically available," says Belda.

The company's current research focus, adds Belda, is to create software based on artificial intelligence that will aid in the creation of new compounds for drug discovery.

The founders of NorayBio, based in Bilbao, saw a need for advanced computations and data analysis in the field of biotechnology. The founders, with experience in biotechnology, chemistry, and research, worked in collaboration with companies and clients to develop software to suit their needs.

Small companies and research groups "were just using an Excel set," says Julio Font, CEO. "Now that's changed; they know they need specialized software for managing data." NorayBio designs software for managing sample banks (such as DNA or tissue samples) that can be tailored to meet a customer's needs.

The company is now developing a visualization system for biomarkers, so researchers can actually see the data in relationship to different biological pathways. The first one in development is software to visualize biomarkers in liver disease. "It's been exciting to see the market evolution," says Font. "Two or three years ago potential customers said they could manage their data with a simple spreadsheet, and now they call and say, 'I need your software.'"

Integromics, a spinoff from the National Center for Biotechnology begun in 2003, has developed a number of solutions to help companies manage and analyze their experimental gene-expression data. The software takes all the information created by a research instrument such as a PCR machine and performs the data analysis for the scientist. The company's founders have focused their sights internationally, and they count companies like Pfizer and Novartis among their clients.

"Usually it takes time for a small company to build up a base," says Marco

system won't allow such a case to be brought to court. "A key differentiating factor between the U.S. and Europe, particularly Spain, is the access to fresh human samples," he says.

Ballesteros left his company in San Diego and brought some of his team to Spain, where in 2007 he founded a new company, Vivia Biotech, with his brother Andres.

Vivia Biotech is partnering with hospitals that have samples of blood and bone marrow samples, and signed consent forms, from leukemia patients. He says his system can test thousands of combinations of the less than a dozen approved leukemia drugs. "We're already seeing tremendous differences" in how different patients' cancers respond to different drug combinations, he says. In theory, a doctor in the future would be able to send his patient's blood in to be tested, and could get an answer back in 24 hours about the patient's best course of treatment.

"This is what doctors have been doing for years, one drug at a time," says Ballesteros. "We're only altering the scale." Ballesteros hopes that this method will be validated within a year.

Ballesteros doesn't stop there. He's particularly excited about the prospect of using this machine to discover new cancer-fighting drugs among existing, approved drugs that treat unrelated diseases.

Most researchers are investigating what genes or proteins differ in cancer and trying to create molecules to kill cancer that don't kill healthy cells, says Ballesteros, "but we do exactly the opposite. We say, let's get all the drugs that don't kill you. And of those, let's see if some of them kill cancer." He ticks off antibiotics, drugs for the flu, for headaches, for Parkinson's. So far, he says, "the data is amazing, much better than what we had expected."

"We've found ten very safe drugs that have the same efficacy in killing cancer as the harmful chemotherapy drugs," he says; but it will take at least three to five years to go through the necessary trials before any will be validated for cancer treatment.

Rodríguez, vice president. "We're lucky in the sense that the software sells itself. Once a client in the lab tries it out, we don't need to explain how much time this can save."

WORKING TOGETHER

The Barcelona Science Park, housed at the University of Barcelona, bustles with constant construction. As soon as companies and research groups fill existing space, more is in demand. The facility is one of the many new research centers in the city that, in partnership with hospitals and local companies, continue to propel Barcelona into the biotechnology future.

Oryzon Genomics, spun off from the Spanish National Research Council and the University of Barcelona, opened its doors in 2001. The company focuses on gene discovery and has developed a high-throughput screening technique to focus on genes of interest, their expression, and their pathways of action.

"The idea in 2000 was that we wanted to develop new applications for discovering key genes in fundamental processes," says Carlos Buesa, Oryzon director and one of the company's founders.

Their technique has allowed Oryzon Genomics to compare tissues. For instance, researchers might compare cancerous tumors to healthy tissue, or diseased brains to healthy ones, to discover the genes or proteins that differ from one to another. The next step for the company has been to discover these biomarkers in more easily accessible samples, such as urine or blood.

Oryzon has several products for early detection of cancer and neurodegenerative diseases based on this technology; in many cases, advanced detection can lead to significantly improved chances of successful treatment. The products in the most advanced stages of development are designed to detect endometrial, colorectal, ovarian, and lung cancers.

This gene screening technique has also led Oryzon Genomics to develop its own therapeutic antibodies, based on their protein discovery. Two are headed for preclinical proof-of-concept trials later this year.

Buesa says its origins in the Barcelona Science Park helped the company on its successful path. "The location was providential," says Buesa. "It was one of the best ideas here in Catalonia [to create a science park] where young companies could be embedded in institutes and share facilities and instruments and equipment, and the creative atmosphere. In the early days we had very little money to invest in instruments and sophisticated facilities."

The Barcelona Science Park is the largest local incubator thus far, home to 50 companies; but an even larger one is under development. "There are 17 science parks in Catalonia, and 9 have activities in life sciences," says Montserrat Daban, head of external affairs for BioCat. The city will also be home to Spain's new genome sequencing center.

Another company housed at the science park is Advancell, founded in 2001 by a group of professors and researchers in Barcelona and Valencia. In 2004 the company launched their nanomedicine unit, the first main product of which is an in-vitro cell reagent to ascertain the oral absorption of chemicals and drugs. The product, called CacoReady, is now entering the North American market.

Advancell has also moved into therapeutics and is developing nano-based medicines for a variety of diseases. They've created nanocapsules for molecules to treat skin diseases such as psoriasis, which greatly improve the delivery and efficacy of existing treatments.

One of the recent products that Advancell has patented began as a solution for an in-house problem. They wanted to send cells to companies, but living cells do not survive freezing and transport well. "We've invented a transport medium, a gel. Instead of being frozen, the cells survive transport alive and well," says Davide Sirtoli, CEO.

Researchers at Biotools transformed a similar challenge into a business opportunity. Their first forays into biotechnology were to produce enzymes for molecular biology applications. But the enzymes and reagents for the process usually needed to be mailed individually at below-freezing temperatures. In response, Biotools created and patented a process in which all the compounds for a complex reaction can be mailed together, semidried, stabilized, and suspended in a gel at just above the freezing point; the addition of water catalyzes the process. Biotools has honed the process for HIV and hepatitis C and is currently working with the government of Brazil to apply the technology around that country for diagnostic testing.

"This was mainly to solve an internal problem," says Sonia Rodríguez, licensing and partnering manager. "We had problems with shipping goods at -20° Celsius. But then we realized this had a greater value."

Diagnostics are the basis of Ingenasa as well. More than twenty years ago, Ingenasa founders focused on the African swine fever virus, a disease that now plagues pig farms across Europe. The company's sensitive diagnostic became a success, leading to diagnostics for close to 80 different products. Ingenasa sells its products to major livestock centers in countries such as China and India. Included in the diagnostics are the robotic and rapid throughput testing systems to analyze tens of thousands of samples in only a few hours..

Today, the company is expanding from their expertise in animal husbandry and moving into human-health products. "We made this decision," says Carmen Vela, Ingenasa's managing director, "because the veterinary field is an interesting and important one, but it's not really the field for making a difference with technological breakthroughs."

Ingenasa has built on its expertise in designing vaccines for livestock viruses. The company has developed a technology that produces a capsid covered in proteins; identical to the virus it is attacking "but not biologically active." "We were able to demonstrate that these capsids can induce very specific T-cell response—and this could lead to the treatment of some kinds of tumors," says Vela.

EVOLUTION OF A COMPANY

Progenika, based at a science park on the outskirts of Bilbao, began when its founders wanted to start a biotechnology company, any biotechnology comany.

So they launched one. "At the beginning we started doing everything," laughs Antonio Martínez, one of the founders. "Food, health, everything."

Martínez had been working for PharmaMar, one of Spain's most established biotechnology companies. His old friend from student days, Laureano Simón, had spent time in Wisconsin and then come back to the National Center for Biotechnology in Madrid. At the time—in the 1990s—there were few opportunities in the Spanish biotechnology sector.

Together with Corina Junquera, Martínez and Simon settled on Bilbao as a home for their new company, because the Basque region had launched an initiative to grow its information-based sector.

"The ultimate goal has been to diversify our industrial tissue and our economy," says Maria Aguirre of BioBasque, the government agency that focuses on the life sciences. The local government's support for biotechnology is intended, she adds, "not just for the creation of new companies, but the creation of jobs to help stay competitive, in areas that have not been traditional for the region."

Progenika set up the new company in Bilbao. Intrigued by the emerging technology of DNA chips, Progenika offered to become a service provider for Affymetrix, a California-based DNA microarray company that provides genetic testing services.

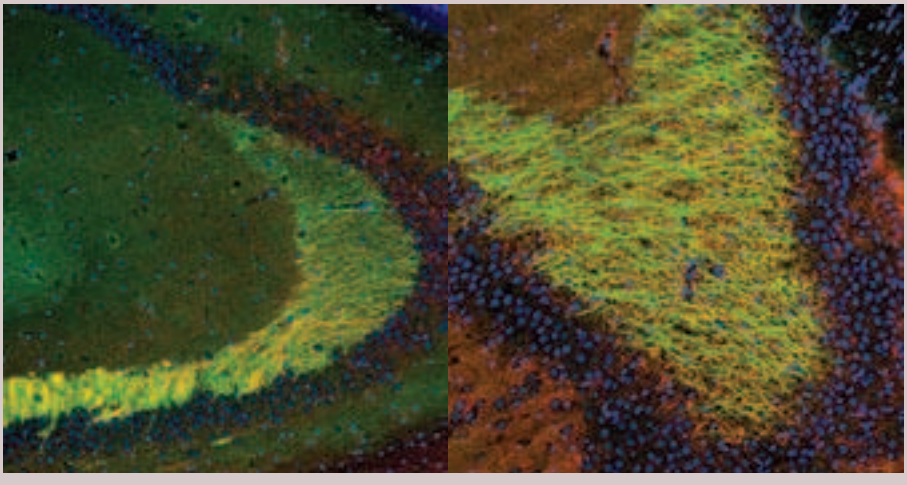
"Providing services is a good way to start, but it's not the way to make Progenika a big company," says Martínez, so the team began to develop its own products.

The Spanish government was interested in identifying people who suffer from familiar hypercholesterolemia (FH), a genetic disease with no visible symptoms that can lead to heart attacks at the age of 40 or 50. The government turned to Progenika for assistance.

The company needed to develop a system to accurately recognize 120 genetic mutations that lead to the disease. After three years of research, in 2004 Progenika received European approval for a diagnostic DNA chip. Newsweek proclaimed it the first genetic diagnostic for FH.

After this success, the European Union approached Progenika to develop a chip to identify blood groups. The two most familiar blood groupings, A/B/O and RH positive/negative, don't represent a variety of other blood groupings more common, for instance, among populations from Africa. Differences can lead to rejection of blood transfusions in patients, who produce antibodies against improperly matched blood.

"The genetic basis of blood groups was not well known," says Martínez. Two years later, the company came out with a DNA chip to test for genetic markers for a variety of blood groupings. They have set up platforms in some of the major blood banks in Spain, the UK and Holland and are beginning to expand into Europe and the Middle East.



Above: Progenika uses mouse neurons in its research into treatment for psychiatric diseases such as schizophrenia. (Source: Dr. Fabien Pichon, Progenika Biopharma 2009)

Progenika continues to research and expand its product lines. It is developing a system to monitor the urine of bladder cancer patients, which can detect proteins from tumors to determine if the tumor is regenerating, as well as diagnostics for Crohn's disease and ulcerative colitis.

Progenika now has 130 people and a vast research space. Says Martínez of the company's rapid growth, "We have a lot of energy. That's important—at the beginning you need a lot of energy."

PHOTO COURTESY OF PROGENIKA

SUPPORTING RESEARCH

Companies such as Advancell and Oryzon Genomics attribute some of their success to government support and to the network of science parks around the country that provide shared facilities for young, smaller companies starting out.

"Science parks have been shown to be one of the best instruments for the creation of technology-based companies in a variety of sectors, including biotechnology," says Felipe Romera, president of the Spanish Association of Science Parks.

The science parks are a key feature of what are known as *bioclusters*, where regional governments such as those in Catalonia, Madrid, Valencia, Andalusia, and the Basque country have invested in coordinating an area's public and private biology research and promoting the creation of knowledge-based companies. These link science parks, hospitals, universities, and private companies to develop a robust biotechnology sector.

"We need to be able to attract talent, and we're seeing a big change in that area," says Montserrat Daban of Catalonia's BioCat. "Many researchers and professionals from the private sector are willing to come here to work, because they see this is a promising sector."

One unusual model of a research institution-company partnership is Digna Biotech, the company created to commercialize research conducted at the University of Navarra's Center for the Study of Applied Medical Research (CIMA in Spanish). Both began operations in 2004.

CIMA, a Pamplona-based research center, studies the areas of gene therapy and liver-related diseases, central nervous system disease, cardiovascular health, and oncology. "Digna's mission is to take the patents from CIMA and move them to the market," says Pablo Ortiz, CEO.

Within only four years, one product has already reached phase-2 clinical trials: a cream for scleroderma, a skin disease with no known treatment. Digna has also developed a treatment that aids in the regeneration of liver tissue after liver surgery and transplant. The treatment goes into clinical trials next year; if successful, it would be the only drug of its kind.

The technology transfer office of the Spanish Council for Scientific Research (CSIC in Spanish) aids in the transfer of patents from more than 6,000 researchers to private companies. CSIC is the largest Spanish research organization, comprising 126 research centers and 145 additional research units associated with local institutions. Under the auspices of the national government, CSIC performs multidisciplinary scientific and technological research to contribute to the advancement of both science and the economy.

The culture in Spain has changed, says CSIC's Beatriz Lara, IP and knowledge transfer manager: "Researchers are increasingly patenting their discoveries and working with companies to develop their research." Her organization helps shepherd researchers through the patent and licensing process.

"It's important to establish a relationship between scientists and companies," says José Pablo Zamorano, deputy director of licensing for life sciences. "Researchers can learn the needs of the private companies, and companies realize there are researchers out there who can help them."

Some challenges remain in the Spanish biotechnology sector. Researchers speak of the need for increased access to venture capital funds. They stress the importance of continuing to develop the culture of patenting innovations and transforming those discoveries into companies. They point out the need to facilitate the creation of companies by university professors, who today are hampered by regulations about how much of a company a professor may own. The Spanish government has a number of initiatives underway to deal with these challenges and encourage the growing industry.

"I think Spain has good competitive advantages in biotechnology," says Joan Ballesteros, chief scientific officer of Vivia Biotech. "There's a lot of great science going on here."

Resources

ICEX (Spanish Institute for Foreign Trade)
www.spainbusiness.com

ASEBIO
www.asebio.com

Biokit
www.biokit.com

Bionostra
www.grupobionostra.com

Genetrix
www.genetrix.es

Oryzon
www.oryzon.com

PharmaMar
www.pharmamar.com

Progenika
www.progenika.com

Vivia Biotech
www.viviabiotech.com

To find out more about New Technologies in Spain, visit:
www.technologyreview.com/spain/

For more information visit:
www.us.spainbusiness.com

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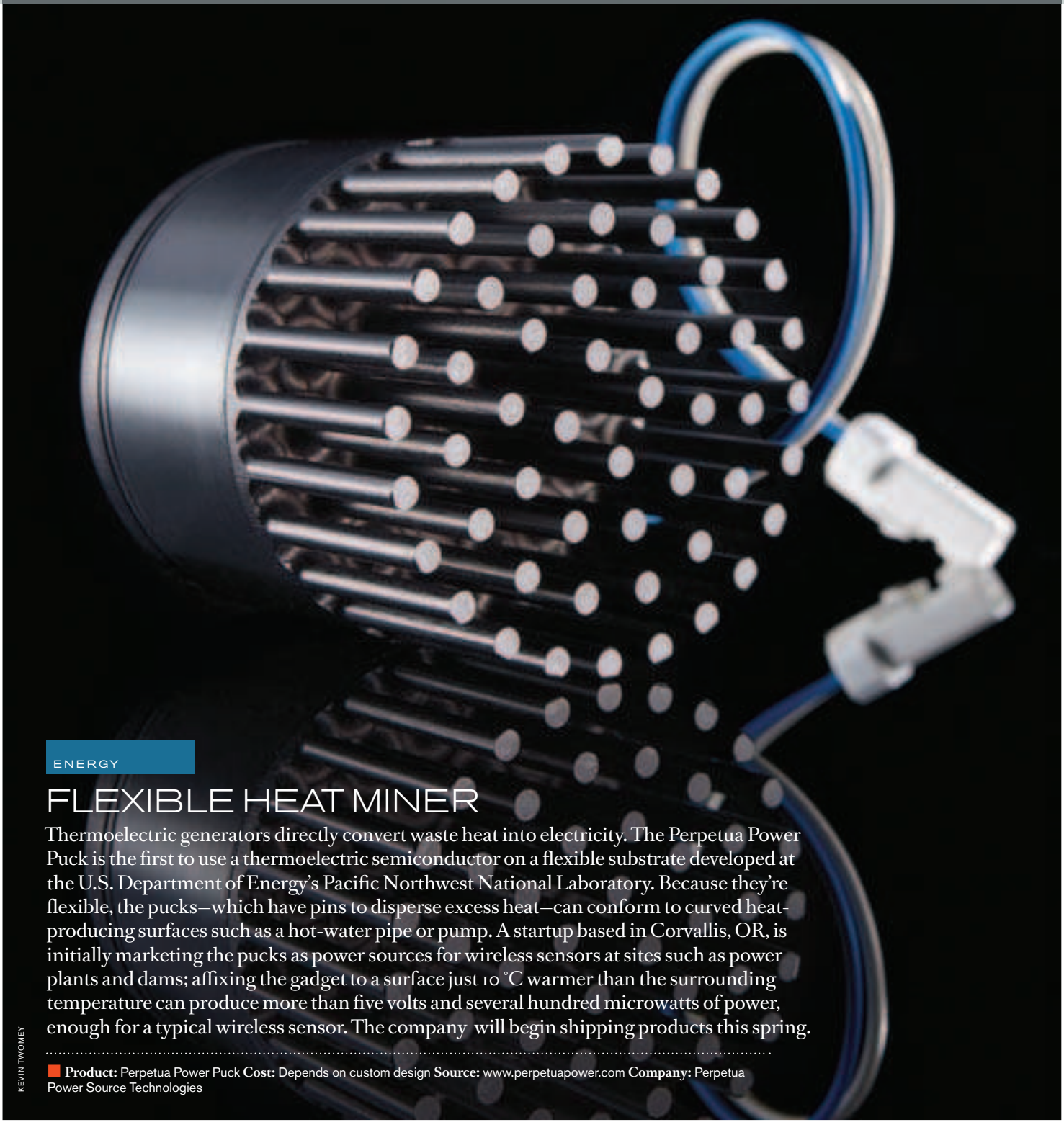
españa,
technology
for life.

TO MARKET



ENERGY

FLEXIBLE HEAT MINER

Thermoelectric generators directly convert waste heat into electricity. The Perpetua Power Puck is the first to use a thermoelectric semiconductor on a flexible substrate developed at the U.S. Department of Energy's Pacific Northwest National Laboratory. Because they're flexible, the pucks—which have pins to disperse excess heat—can conform to curved heat-producing surfaces such as a hot-water pipe or pump. A startup based in Corvallis, OR, is initially marketing the pucks as power sources for wireless sensors at sites such as power plants and dams; affixing the gadget to a surface just 10 °C warmer than the surrounding temperature can produce more than five volts and several hundred microwatts of power, enough for a typical wireless sensor. The company will begin shipping products this spring.

KEVIN TWOMEY

Product: Perpetua Power Puck **Cost:** Depends on custom design **Source:** www.perpetuapower.com **Company:** Perpetua Power Source Technologies

COMPUTING

Quick Booter

TIRED OF waiting, seemingly without end, for your computer to boot up? Software called Presto could make your life a lot more pleasant. A handful of products already make it possible to start a computer in seconds, but unlike the competition, Presto doesn't need to be integrated into a computer's hardware by the manufacturer. Simply download Presto—essentially a stripped-down Linux operating system—and within 10 seconds of booting up the system, you can get online to do simple things like check e-mail, use Skype, and send instant messages. Presto became available in April.

Product: Presto **Cost:** $19.95 **Source:** www.prestomypc.com **Company:** Xandros

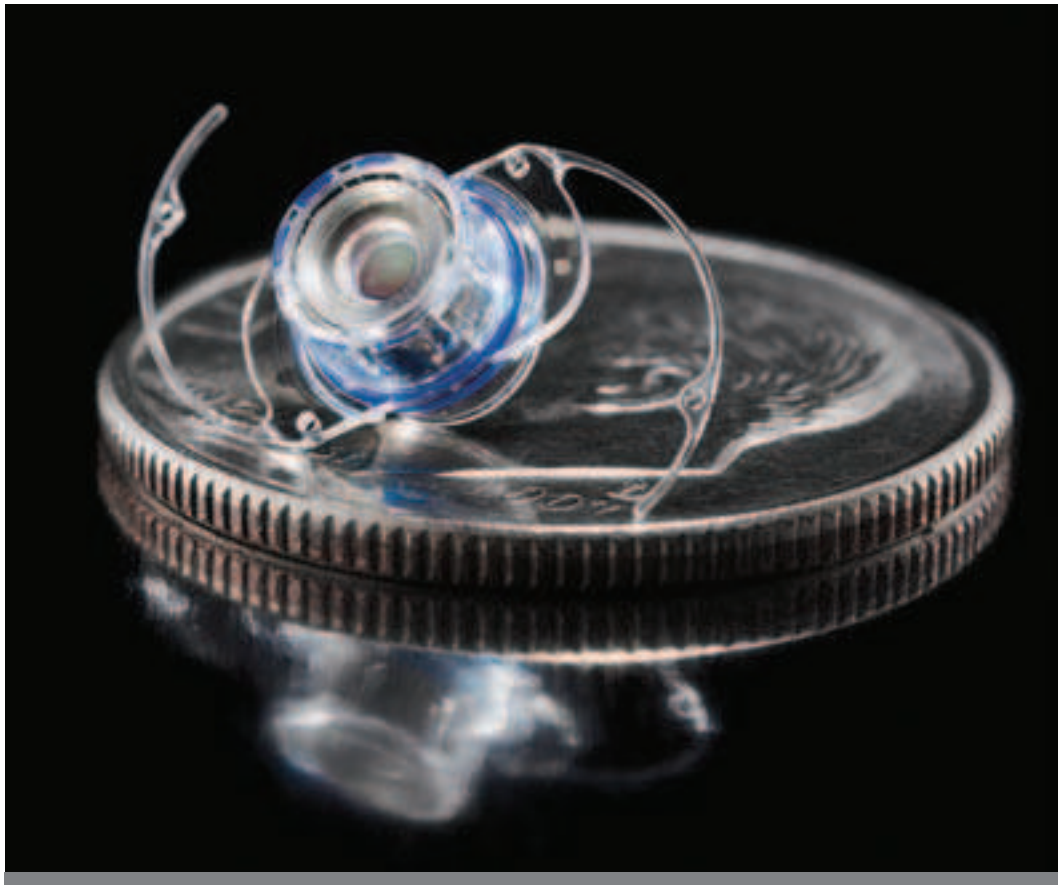
PRINTING

TONER REPLACEMENT

"SOLID INK" is melted in a print head and jetted through tiny nozzles onto paper, where it rehardens. Compared with printer toner, the technology is cheaper, produces sharper colors, and requires less energy. But until recently, it has worked only in low-speed printers. A new print head from Xerox (right, atop ink blocks) will now make high-speed solid ink-jet printing possible for office and commercial uses. It's a block of stainless steel with a web of channels and tunnels that distribute ink to 880 individual nozzles, each 40 micrometers wide. A forthcoming Xerox color printer and copier with four such gadgets, spewing more than 150 million drops per second, will use 30 percent less energy than laser printers, reduce the cost of color copies, and banish messy toner cartridges.

Product: Solid-ink color printer and copier
Cost: To be announced in late spring
Source: www.xerox.com
Company: Xerox

COURTESY OF XANDROS (PRESTO); KEVIN TWOMEY (PRINTER)



MEDICAL DEVICES

IMPLANTABLE TELESCOPE

AN IMPLANTABLE mini-telescope could help restore visual acuity to people with macular degeneration, a progressive disease that affects the center of the retina. The device, which is smaller than a pencil eraser and can be implanted during an outpatient procedure, works a bit like a telephoto lens in a camera: it enlarges the image that falls onto the retina so that it extends beyond the damaged area. In human studies, 60 percent of patients could read at least three lines further on an eye chart after the telescope was implanted. The device is approved for use in Europe, and an advisory panel for the U.S. Food and Drug Administration has unanimously recommended approval.

Product: Implantable Miniature Telescope **Cost:** Not available **Source:** www.visioncareinc.net **Company:** VisionCare Ophthalmic Technologies

ELECTRONICS

Portable Electrocardiography

A COMPACT heart monitor from GE Healthcare weighs just three kilograms, far less than today's 29-kilogram versions. The device includes a phonelike keypad, a full-size color display, and diagnostic software. It received approval from the U.S. Food and Drug Administration this spring and will be sold here later in the year; the target market will be doctors' offices and remote healthcare clinics. The gadget is already used in rural India and China.

Product: MAC 800 **Cost:** approximately $2,500 **Source:** gehealthcare.com **Company:** GE Healthcare

NETWORKING

HD OVER WI-FI

MANY HOMES have Wi-Fi routers, but commercially available routers aren't reliable for applications such as streaming high-definition video. Startup Quantenna Communications hopes its Wi-Fi technology will change that. Its chipset makes it possible to employ beamforming, in which a high-bandwidth stream of data can be directed toward a specific device, such as a television—something not possible with standard Wi-Fi routers. The result is a wireless connection with effectively double the range and bandwidth. The device will be available later this year.

Product: QHS100 chipset
Cost: Not available
Source: www.quantenna.com
Company: Quantenna Communications

KEVIN TWOMEY (IMPLANT); COURTESY OF GE HEALTHCARE AND QUANTENNA (EKG & WIFI)

DISPLAYS

NEW E-READERS

THE LEADING electronic readers, Amazon's Kindle and Sony's Reader, have greatly increased interest in e-books but share a couple of limitations: they are rigid, and they display only in black and white.

Earlier this year, startup Plastic Logic introduced an e-reader that uses polymer electronics to create a flexible display that is the size of a standard sheet of paper. Coming next are two e-readers that will offer some benefits previously missing: one features a color display, and the other is a pocket-size gadget with a screen that rolls up.

ROLL-UP READER

THE READIUS, made by Philips spinoff Polymer Vision of Eindhoven, the Netherlands, is the size of a cell phone and sports a rollable screen that stows away. The display uses the same black-and-white microcapsule display technology that's used in the Kindle and the Sony Reader, but the capsules are applied to paper-thin flexible plastic and controlled by electronics made of polymer organic semiconductors. The Readius is expected to reach market later this year.

Product: Readius **Cost:** Not available **Availability:** Later this year **Source:** www.readius.com **Company:** Polymer Vision

Reading in Color

THE FLEPia, made by Fujitsu, is the first color electronic reader to hit the market. Its screen technology is a stripped-down version of traditional liquid-crystal displays. Instead of using a backlight, it reflects ambient light from red, blue, and green crystals arranged in separate layers (in conventional LCDs, the three colors sit side by side). The crystals are arranged in a way that makes them transparent when not in use; electric currents change their orientation to make them reflect different colors. The reader has a touch screen that can be used with a stylus. The device was scheduled to go on sale in Japan in April.

Product: FLEPia **Price:** about $1,000 (99,750 yen) **Source:** www.frontech.fujitsu.com **Company:** Fujitsu

COURTESY OF POLYMER VISION AND FUJITSU

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DIAGNOSTICS

BLOOD TEST FOR DOWN SYNDROME

TESTS CURRENTLY used to determine whether an unborn child has Down syndrome carry a small risk of miscarriage, but a new test for the genetic abnormality could solve that problem by getting results from a maternal blood sample. The test, expected on the market this year, analyzes fetal RNA and DNA in the maternal blood serum for specific genetic markers found on chromosome 21. The number of copies of each of these markers reveals whether the fetal DNA has an extra copy of the chromosome—the genetic variation that causes Down syndrome.

Product: SEQureDx
Cost: Not available
Source: www.sequenom.com

COMPUTING

A TOUCH NETBOOK

NETBOOKS—pint-size laptops for Internet access and light computing such as word processing—have grown in popularity and variety. Now a detachable netbook allows users to remove the screen from the keyboard and use it as a touch-screen tablet computer. The device, which weighs 0.9 kilograms, includes batteries in each half; the detached tablet runs for about four hours on its batteries, while the combined tablet and keyboard lasts ten hours. The gadget uses a processor normally found in smart phones and BlackBerrys. It is expected to reach market this summer.

Product: Touch Book **Cost:** $399 for whole system, $299 for tablet alone. **Source:** www.alwaysinnovating.com/store
Company: Always Innovating

MOBILE DEVICES

Movie Phone

Friends no longer have to gather 'round the laptop to watch the latest YouTube video. A Samsung phone doubles as a projector, displaying still or moving images up to 1.2 meters wide. The phone incorporates digital light-processing technology from Texas Instruments, in which images are projected by hundreds of thousands of microscopic mirrors in an array. Samsung plans to release the phone in Europe this summer; it's already available in Korea.

Product: Samsung I7410, W7900 **Cost:** Not available **Source:** www.samsung.com
Company: Samsung

KEVIN TWOMEY (TOUCH BOOK); COURTESY OF SAMSUNG (PHONE)

SPOTLIGHT ON INNOVATION

A TECHNOLOGY REVIEW CUSTOM SERIES

The Technology Review Custom Team takes a look at the technologies that are changing the way we live and do business.

The last of four articles focuses on groundbreaking UAV and AUV technology and what that means—not only for the Defense Department, but also for scientific research. To read the complete Spotlight on Innovation series—including articles on clean energy, mobile technology, and personalized medicine—visit www.technologyreview.com/spotlight.

MAVERIC PHOTO COURTESY OF PRIORIA ROBOTICS, INC.

ZOOMING INTO THE FUTURE

The vehicle glides over the rough Afghan terrain, scanning for militants and insurgent troops in training. Thousands of miles away, in Nevada, a soldier helps the plane navigate the chosen course.

The unmanned aerial vehicle (UAV) represents one of the latest examples of high-tech equipment increasingly in demand in battle zones such as Iraq and Afghanistan. The vehicles are also serving both security and civilian purposes here in the United States, such as zooming along the edges of forest fires or hovering in clouds to collect atmospheric activity.

Autonomous underwater vehicles (AUVs) are being designed to serve similar security and civilian purposes, but in a marine environment; to test for chemical plumes or evaluate oil spills; to investigate potential terrorist threats from ships; and to conduct scientific surveys of underwater environments.

VISION AND JUDGMENT

One significant problem in designing fully autonomous unmanned vehicles is the capability to recognize objects in the environment and judge how to respond.

Prioria Robotics, a small company located near the University of Florida, in Gainesville, has partnered with the university UAV lab to find solutions to this problem. Prioria has developed image-processing technologies to help a small plane "perceive the world around it," says CEO Bryan da Frota. The company mounted its system on Maveric, a mini-UAV with a 29-inch wingspan that Prioria launched into the market in early 2008.

Maveric's capabilities, says da Frota, are sophisticated enough for a semi-urban situation: they avoid groups of buildings or trees and adjust to shifts in terrain. A dense urban center such as downtown Manhattan, however, would prove too complicated for Maveric's current navigation system. Prioria has already sold the UAVs both domestically and internationally and is working on refining and improving the collision-avoidance system.

EVALUATING THE WATER

Similar challenges exist for marine systems. GPS signals, which serve well for aerial vehicles, cannot penetrate underwater. The Marine Technology Program at SRI International, based at the research institute's St. Petersburg, FL, branch, is working on advanced systems that allow underwater vehicles to precisely navigate without GPS.

SRI is also working on sensors that are smaller and cheaper, and demand less energy. Says Larry Langebrake, director of SRI, "You need a mission controller onboard the vehicle that has enough computing capability that it can take multiple sensory input, such as position and chemical composition, and use those together to make decisions." Those computing needs require increased power, and miniaturized low-power sensors could free up power for use elsewhere in the vehicle. SRI has already employed its AUVs and sensors in fisheries research and has mapped and catalogued a Civil War–era steamship off Florida's west coast.

COMPREHENDING THE WORLD

Today's aerial vehicles can send streaming video back to a central control. In the future, soldiers in battle or police officers in a city hope to have vehicles capable of autonomously analyzing video and alerting the attending soldier or officer to a potential threat.

This is the challenge that Mubarak Shah, director of the computer vision lab at the University of Central Florida (UCF), is trying to tackle. His lab is developing a system that not only records video, but can also recognize behaviors such as violence, the movement of people falling down due to a chemical attack, or figures running from a threat.

"The approach is to train the system to recognize example behavior," says Shah. "We'll have someone running, and then train the system to learn what that is so it can report back, 'I saw running.'"

This type of system exists in a fixed land-based video, but developing an equivalent for moving aerial vehicles presents additional computational challenges. Shah's UCF lab has received Defense Department research funding and is partnering with companies such as Lockheed Martin.

The potential for security applications, law enforcement, and research is vast, and scientists are getting closer to making it a reality.

Continues online:
Read the complete article online at www.technologyreview.com/spotlight.

SOFTWARE

VIDEO ENHANCER

MANY VIDEOS on YouTube are of terrible quality: the resolution is low, the lighting's bad, and often the camera work is jerky. Now, new software for PCs offers consumers their first access to "super-resolution" algorithms used by the CIA to enhance low-quality video. The software enhances individual frames after analyzing and extracting information from multiple surrounding frames. In addition to improving resolution, the software can also remove noise, brighten dark areas, sharpen blurry scenes, and stabilize shaky ones.

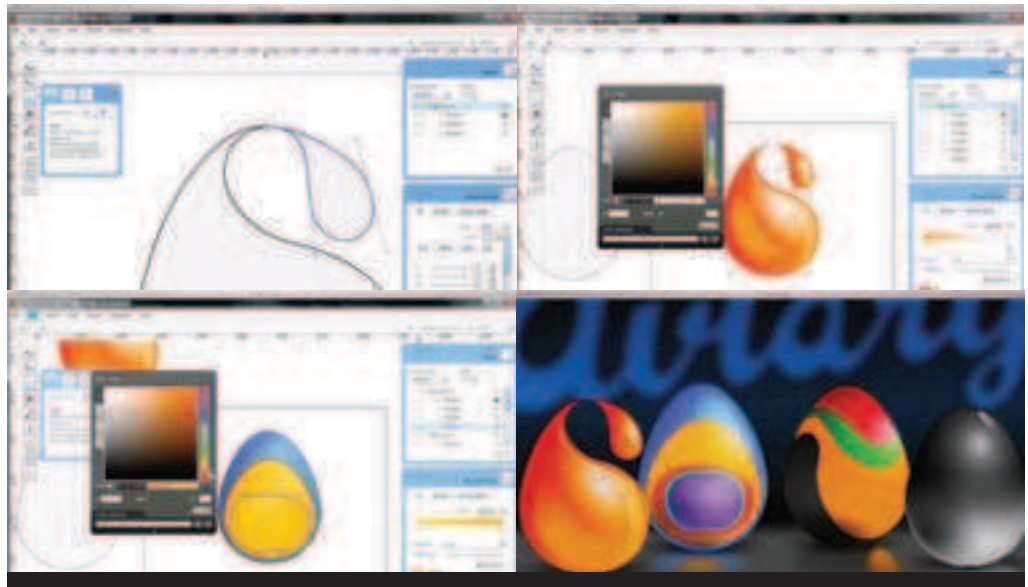
Product: vReveal
Cost: $49.99
Source: www.vreveal.com
Company: MotionDSP

ENERGY

Greener Laptops

HEWLETT-PACKARD is offering a faster-charging and longer-lasting lithium-ion battery for 18 of its laptop models. The underlying technology comes from startup Boston Power, of Westborough, MA, which completely redesigned the cells in these batteries—a process that involved changing their shape and chemistry. Where other lithium-ion batteries typically lose half their charging capacity in just one year, the Boston Power batteries retain 80 percent of their original charge after three years. They charge 50 percent faster too.

Product: HP Enviro Series laptop battery **Cost:** $149.99 **Source:** www.shopping.hp.com
Company: Hewlett-Packard, Boston Power



WEB APPLICATIONS

DRAWING ON WEB RESOURCES

SOPHISTICATED TOOLS for creating top-quality digital art are now available free through a Web application. With Raven, users can create complex illustrations based on vector graphics, in which formulas are used to render images that can be scaled to any size without losing detail. The market for this technology, which grounds much of today's professional digital graphics, has been dominated by Adobe Illustrator. Ironically, Raven's sophistication is possible partly because the application was created in Flex, an open-source framework for Web applications that's also built by Adobe.

Product: Raven **Cost:** Free **Source:** aviary.com **Company:** Aviary

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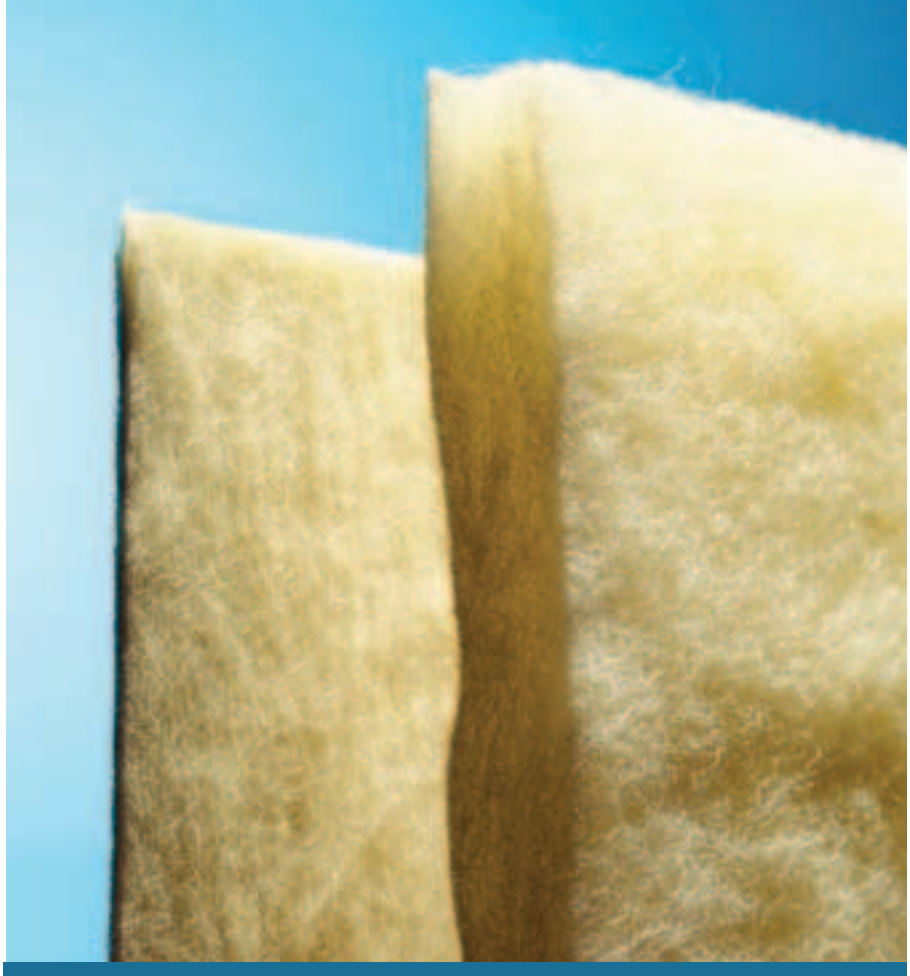

MATERIALS

SMART INSULATION

MANY FIREFIGHTING uniforms contain an insulating material trade-named Nomex, a polymer made for decades by DuPont. The company has now developed a new version of Nomex that is thin and comfortable in everyday use, but grows three to four times thicker when temperatures rise above 121 °C, providing a 20 percent boost in thermal insulation. In March, DuPont began marketing the material in North America as a liner for firefighters' jackets; the company will market it globally by year's end.

Product: Nomex On Demand **Cost:** The company estimates that the material will add $50 to $100 to the price of a firefighter's suit **Source:** www.dupont.com **Company:** DuPont

TRANSPORTATION

Crash Avoider

SOME LUXURY cars already come equipped with a radar unit mounted inside the grille that maintains a fixed distance behind the car ahead; it has the capacity to ease the throttle and even brake lightly. An enhanced version coming to market later this year serves as a crash-avoidance system. It combines visual and radar sensors (above) with advanced vision-processing software to detect moving vehicles and stationary objects up to 170 meters away, and pedestrians 30 meters distant. The system sounds an alarm when braking is necessary; when it senses an imminent collision, it can apply full braking if the driver fails to do so immediately. The technology will appear in the 2010 Volvo S60 and several other models in North America.

Product: Electronically scanning radar
Cost: Included in vehicle prices
Source: www.delphi.com.
Company: Delphi

SENSING

EARLY WARNING FOR HEATSTROKE

A NEW DEVICE FOR football helmets warns of the dangerous spikes in body temperature associated with heatstroke. The device consists of a rugged sensor (the black object visible at the left side of the helmet), encased in a headband or helmet cushion, and a transmitter that beams temperature readings wirelessly to a PDA on the sidelines. If the wearer's body temperature reaches and sustains a reading of 39 °C for more than 20 seconds, an alarm goes off on the PDA.

Product: Heat Observation Technology System **Cost:** $99 per player for a team system **Source:** www.hotheadsports.com
Company: Hothead Technologies

KEVIN TWOMEY (INSULATION); COURTESY OF DELPHI (CRASH); COURTESY OF HOTHEAD (HELMET)

Technology Review's Career Resources

Do you want to take the next step toward professional growth? Career Resources brings you success stories from executives who continued their education, essential advice from experts on how to achieve your career goals, and a directory of programs designed specifically for the working professional. **www.technologyreview.com/careerresources/.**

Career Growth Profile

Foster Hinshaw

Age: 61

Job Title: CEO and President

Employer: Dataupia.

Graduate Programs: MS, engineering, Cornell University, 1971; MBA, Harvard University, 1974

Foster Hinshaw, the founder, CEO, and president of Dataupia, understands the power of information. Through technology, his company helps businesses affordably streamline and quickly access massive amounts of data so they can operate with greater insight and efficiency. It's the perfect challenge for Hinshaw, an enterprising engineer with a head for business.

While some tech industry executives wait until midcareer to earn advanced degrees in business or management, Hinshaw knew as an undergraduate at Cornell University that his schooling should go beyond engineering formulas and equations.

"Apart from engineering, I have always had a strong interest in strategic and nontechnical issues, and I knew I wanted to combine these interests," he says. "I learned from the experiences of my engineering-school classmates that the path out of engineering and into business without an MBA was difficult. To become successful and hone my business skills, it was clear that I would need to further my education outside of engineering with an MBA."

Upon finishing his bachelor's and master's degrees in engineering, Hinshaw applied for and was accepted to the MBA program at Harvard University. Almost every summer during his college years, he worked to pay for his degrees. He started out in tech positions, working at Pan Am as a radio technician and at Hewlett-Packard as an engineer. "The inside knowledge I gained from being on the tech side in those early years of my career definitely deepened my understanding of how to make successful and impactful business decisions in tech-based companies later on," he says.

Armed with an MBA, Hinshaw ventured into the business world in 1974. He has worked almost exclusively with small companies and startups ever since. His first job with a startup was as an engineer for Electric Fuel Propulsion, a manufacturer of full-sized electric cars.

Hinshaw also spent several years as a consultant on large data systems and e-commerce applications for tech companies. Then he served as a Y2K practice manager at Keane before moving on to become the chief financial officer and director of information systems for VideoGuide (now part of TV Guide).

To learn more about Foster's decision to continue his education—and how it helped him move up the corporate ladder, visit **www.technologyreview.com/careerresources/.**

Program Directory

ENERGY

BUYING GRID INTELLIGENCE

TODAY'S electricity grid—and the buildings and appliances it powers—are, for the most part, dumb. In most areas, there's no way for utilities and consumers to communicate in real time, so it's difficult to reduce demand during peak times. The stimulus bill passed early this year provided $11 billion to upgrade the grid, but it's going to take a while. In the meantime, a growing number of technologies are available for consumers who want to understand and manage their electricity consumption. Here are some of the latest products.

Smart Fridge

MANY UTILITIES are considering tiered pricing systems based on demand at different times. GE's smart refrigerator and other appliances going on sale this year can connect with energy management systems to receive real-time pricing information and do things like delay a defrost cycle until prices go down. Washing machines and dishwashers can also delay operation or switch to efficient modes. Customers can override these cost-saving functions if needed.

Product: Energy-management-enabled appliances
Cost: Not available
Source: www.geconsumerproducts.com
Company: GE

HOME MANAGEMENT SYSTEM

A MOBILE application from Tendril, a startup in Boulder, CO, will make it possible to control appliances and heating-and-cooling systems from an iPhone. The app is designed to work with Tendril's smart outlets (which monitor and control individual appliances and lighting) and smart thermostats (which allow fine-grained control of furnaces and air conditioners). These devices communicate wirelessly to an Internet-connected household hub, through which they can be controlled via the iPhone or any other means of Web access. They also enable utilities to tweak electricity loads, with customers' permission.

Product: Vantage Mobile **Cost:** Included in the $100 typical cost for initial setup of Tendril's energy-management system **Source:** www.tendrilinc.com **Company:** Tendril

Grid Control Box

SENSORS can measure the performance of transformers and power lines, allowing utilities to respond to breakdowns and spot opportunities to save energy. But such devices often require costly proprietary communication networks. SmartSynch's SmartBox communicates with just about any grid-monitoring equipment and sends the data through existing cellular networks, paving the way for wider adoption.

Product: DCX SmartBox **Cost:** Available on request **Source:** www.smartsynch.com **Company:** SmartSynch

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Q&A

THE SILVER LINING

Entrepreneurialism and innovation during a recession

These are tough days for entrepreneurs seeking new cash, and even for venture capital firms that may be forced to conduct triage on existing portfolios. Still, now may be just the moment to turn a great idea into a lasting enterprise. That was the take, anyway, of venture capitalists and entrepreneurs who gathered in Silicon Valley earlier this year to talk about why recessions are the best times to launch companies and topple old orders.

Steve Jurvetson, managing director of the venture capital firm Draper Fisher Jurvetson, and Dave Goldberg, former manager of Yahoo Music and entrepreneur-in-residence at Benchmark Capital, explained that while a world of failing corporate titans and changing government policy is chaotic, chaos creates opportunity and leaner times bring focus. Jurvetson and Goldberg were joined by three entrepreneurs who described their travails and coping strategies in their recently launched ventures.

They are Krishna Subramanian, cofounder of Mobclix, which helps iPhone developers monitor and profit from their apps; Leah Culver, who founded the now-defunct microblogging site Pownce (she's now developing social technologies at the blogging site Six Apart); and Sol Lipman, cofounder of 12seconds, which he hopes will do for short videos what Twitter did for text.

Jason Pontin, editor in chief and publisher of *Technology Review*, moderated the discussion at a February gathering in Mountain View, CA, sponsored by the Churchill Club, a Silicon Valley business and technology forum. Edited and condensed excerpts from the event follow.

Jason Pontin: Why start a venture now? To many, it might seem like the worst of times. And yet, as Steve will tell you, there are good examples from history that suggest that now may be a very good time to start a company.

Steve Jurvetson: The *best* time. Certainly from an investor's standpoint, there's perhaps no better time to be investing in startups. The entrepreneurs doing it are pretty passionate about what they do. Companies raised with scarce resources tend to be more resourceful, right?

This tends to form the DNA of the firm early on. Some companies, like Hewlett-Packard, are still frugal to this day, largely tracing back to their roots. ... It's also the case that startups thrive in disruption.

Big companies falling on their swords left and right create opportunities for new entrants. It's almost like a forest fire has cleared out the old-growth trees and now prairies can grow again, and new entrants and new species. If you're [electric-car startup] Tesla, for example, what better time to compete with General Motors and Chrysler?

JP: Sol, why did you decide to start your venture now?

Sol Lipman: We were looking for funding in September. It was a very difficult time; it's still a very difficult time. In October I said, "We're not going to go looking for any more funding," because I was spending 80 percent of my time looking for funding instead of focusing on my product and doing a kick-ass job. As soon as we started focusing, we started succeeding. And I think that is the key to succeeding in this recession. ... Yes, you're going to work about a thousand times harder than you generally do, but you're passionate and you're there for the journey.

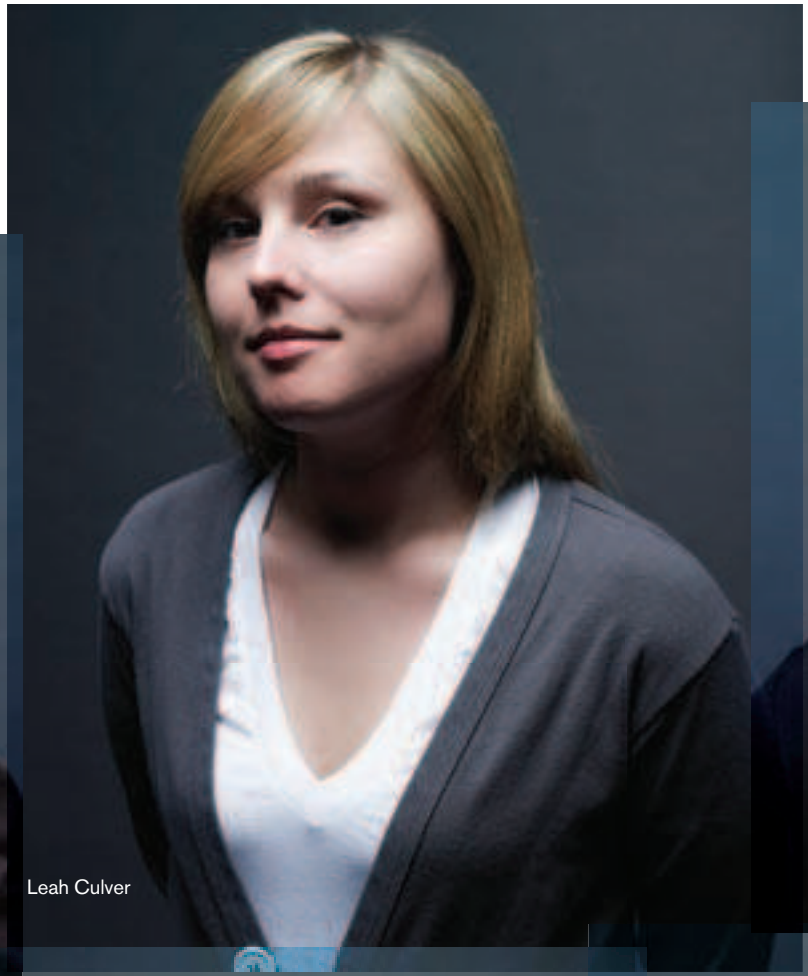
So when we do go to raise money, I think that (a) our company is going to be more valuable, and (b) we're going to understand our revenue model. We're going to have traction. We're going to be in a way better position. And we will have—as Steve said, we're going to have a culture of frugality.

Krishna Subramanian

JP: Krishna, why launch a company now?

Krishna Subramanian: There's tremendous talent around. There are always people looking to leave some of these larger companies that are really talented, and they have been almost like in a cave, just waiting to explode.

Photographs by JEFF SINGER



Leah Culver

Dave Goldberg

Sol Lipman

Steve Jurvetson

I mean, if you're going to do it, you might as well do it now.

Dave Goldberg: [Until] probably a year, year and a half ago, capital was cheap. It made sense to take that money. But the capital being cheap made everything else expensive. And so talent, real estate, advertising, and anything you needed to do to build your business was really expensive. Everyone had access to cheap capital. And now we just flip that around. What these guys are saying is that everything else now is cheap. You probably can negotiate to get free rent if you really need it.

JP: You're not going to raise capital?

DG: I'm not going to raise venture capital for this business [developing an online music-licensing system], because this business doesn't really need that expensive level of capital for the scope of business that we're trying to build.

"IF THIS IS A SCARY TIME FOR VENTURE CAPITALISTS WHEN IT COMES TO THE CONSUMER INTERNET, RIGHT NOW IS THE BEST TIME EVER FOR DEVELOPERS. EVERYTHING IS SO CHEAP. AND HOW ARE THE VCS FEELING ABOUT *THAT*?"
LEAH CULVER

A year and a half ago, would I have taken it if it were cheap? Probably. You have to be able to be flexible about these things. But I'm happier this way, because everything else I'm doing got cheaper, so I didn't need the capital.

JP: So every single one of these people—including Leah, who has gone to work for a larger company—isn't raising capital. No one wants your money, Steve.

SL: That's not true!

JP: Well, Sol wants your money.

Leah Culver: If this is a scary time for VCs when it comes to the consumer Internet, right now is the best time ever for developers. Open-source software has got to the point where you can build highly scalable systems. Cloud computing is cheap. Everyone from Amazon to Microsoft is now providing cloud computing, and it's awesome. So for the consumer Internet, it's really been like this great, great thing. Everything is so cheap. And how are the VCs feeling about *that*?

SJ: We're finding that we're writing a lot of smaller checks for the Internet companies, and that's great. We actually like that.

JP: One of the most striking things about this market is that liquidity events, the exit strategies for which VCs look—initial public offerings and acquisitions—are very uncertain. How do VCs manage their investments when they don't know how they will get their money out?

SJ: There are two layers of difficulty. It's the worst time to be forcing a sale of a startup, which you couldn't do if you tried. You shouldn't be seeking liquidity just for its own sake. And then, within the venture firm there could be a separate problem. ... You've drawn down all the capital that was available and yet you're still waiting for those IPOs. There's a triage exercise some firms are going through.

DG: This is the more fundamental problem in the venture business, and it affects the investment strategy. It's not just at Benchmark. A lot of firms at any other time would already be public—great firms, profitable, growing nicely. But there's no public market for these firms. And so you're left with an M&A [mergers and acquisitions] decision which may not be there. ... This might be the time we lose a lot more of the weaker [venture] firms.

JP: [*Looking at the entrepreneurs*] Do you think about exit strategies at all?

"IF YOU WANT TO BE AN ENTREPRENEUR, THE BEST THING TO DO IS FIGURE OUT, CAN YOU SELL PEOPLE ON A DREAM AND A PASSION? YOU'VE GOT TO HAVE OTHER SKILLS, BUT IF YOU CAN'T DO THAT, IT'S TOUGH TO BE AN ENTREPRENEUR IN A GOOD OR BAD PERIOD."
DAVE GOLDBERG

SL: We think about the exit strategy all the time. You need to have a goal in mind, you need to visualize and think about it every single day. However, the value creation happens on a day-to-day basis. We really actually focus on doing our job day to day.

JP: We've all said airily that recruitment is easier during a recession, because people are available; but it's also difficult, because stock options aren't very appealing when there are no IPOs. Leah, how did [CEO] Chris [Alden] attract you to Six Apart?

LC: You're going to put me on the spot? Six Apart makes lots of money, providing services for media and professional, big bloggers. They are hoping to really turn over this year and become profitable. Can't talk too much about it.

KS: Lucky for us, the iPhone has been really hot, and a lot of people are trying to get into the mobile-application space. We've been lucky enough to find talented people from some of the large firms.

DG: If you want to be an entrepreneur, the best thing to do is figure out, can you sell people on a dream and a passion? Because if you can, that's probably one of the biggest qualifications. You've got to have other skills, but if you can't do that, it's tough to be an entrepreneur in a good or bad period.

JP: When you have too much money, you can fund every crazy idea. Can having too little money be a salutary discipline?

SJ: We were trying to find out what correlates with success or failure in a portfolio. The one correlation [with failure] that held through up and down was the size of the series A—the first round of funding. The bigger it was, the more likely the company was going to fail.

SL: I think the economy has done every entrepreneur a big favor, by making you focus, making you know what you want. The point is to go do something. It's not the exit, it's not the money—it's to do the thing that's there for you to do.

JP: Entrepreneurs: the disinterested artists of the business world! None of the entrepreneurs [here] took angel funding. Did any of you consider it?

KS: Angel funding is definitely something we are very interested in, especially in this market where we are able to take a smaller amount of angel funding, where the exit size might not be as large as it might have been five years ago. A lot of the professional angels do come with contacts, and open a lot of doors.

LC: The ones who have the big pocketbooks in good times tend to be keeping their money close now.

"I THINK THE ECONOMY HAS DONE EVERY ENTREPRENEUR A BIG FAVOR, BY MAKING YOU FOCUS, MAKING YOU KNOW WHAT YOU WANT. THE POINT IS TO GO DO SOMETHING. IT'S NOT THE EXIT, IT'S NOT THE MONEY—IT'S TO DO THE THING THAT'S THERE FOR YOU TO DO."
SOL LIPMAN

JP: If it's true that recessions are often periods when great ideas are turned into lasting enterprises, what are those ideas?

SL: Twitter!

SJ: I don't think there's one elephant in the room—there are a lot of mammals, and I'd bet on the whole field.

DG: We are marginally through the transition of the media business from the physical to the digital. Obviously, people see that the first thing to go away is the physical newspaper. ... We are still very early on, and video is probably the biggest part of that.

LC: Omigosh. Phones: make them smaller, get there faster. Please hurry up. I want to watch videos on the phone. I want to check in with friends on my phone, I don't want to own any other device. Just get there, please.

JP: In the developing and poor world there are a whole host of problems calling out for elegant solutions. There are real markets and money to be made, but they are also places where technology can truly improve human lives. Are any of you interested in creating technologies for India, China, or Africa?

SJ: There are so many needs on the planet. A subset of that is water purification—probably the biggest mismatch between a screaming, enormous market and a lack of technology innovation I've ever seen. This is a trillion-dollar opportunity, and that's just water purification.

The U.S. government's stimulus package *(see "Can Technology Save the Economy?" p. 44)* means that a lot of money is about to pour into Silicon Valley and places like it. Will people know what to do with it?

SJ: Some of Obama's efforts are going to funnel a lot of money into startups. A lot: several hundred million dollars. And I don't think it's entirely a good thing.

WWW Watch highlights of the Churchill Club discussion: **technologyreview.com/churchill**

Audience: But will you leverage capital with government stimulation capital?

SJ: Yes, in certain companies. There are some companies involved with solar thermal and solar installation that used to rely on tax-equity investment [in which state or federal governments provide tax incentives for funding renewable-energy projects].

Now there is a new plan in place that is even better than we'd dreamed of. We

"MOORE'S LAW DOESN'T PAY ANY ATTENTION TO A RECESSION OR DEPRESSION. SO YOU HAVE ALL THIS PENT-UP INNOVATION THAT WILL FIND A WAY TO REVOLUTIONIZE INDUSTRIES. NEW-COMPANY FORMATION IS THE ECONOMIC JUGGERNAUT OF THE FUTURE."
STEVE JURVETSON

didn't lobby for it, we never asked for it, but from our perspective it will create a boom in solar installations of all sorts. We don't invest in companies with the hope of a handout, or the hope that the government will swoop in and create a regulatory regime that is noncompetitive.

But when it happens, then it's a windfall, and it's not like we're going to turn it away. The only problem is that you can't predict the next one. Moore's Law doesn't pay any attention to a recession or depression. ... So you have all this pent-up innovation that will find a way to revolutionize industries.

Startups and new-company formation are the economic juggernaut of the future—always have been, always will be. TR

T. GREGORY GUZIK

The advanced thin ionization calorimeter (ATIC), a balloon-borne instrument, is used to detect bursts of cosmic rays that may be evidence of annihilating collisions between dark-matter particles. ATIC is flown at McMurdo Station on Ross Island in Antarctica, where summer wind patterns carry the detector on a long flight around the South Pole. On this page, workers prepare the balloon for takeoff at McMurdo in 2005; on the facing page, ATIC is tested before the 2007 launch.

PHOTO ESSAY

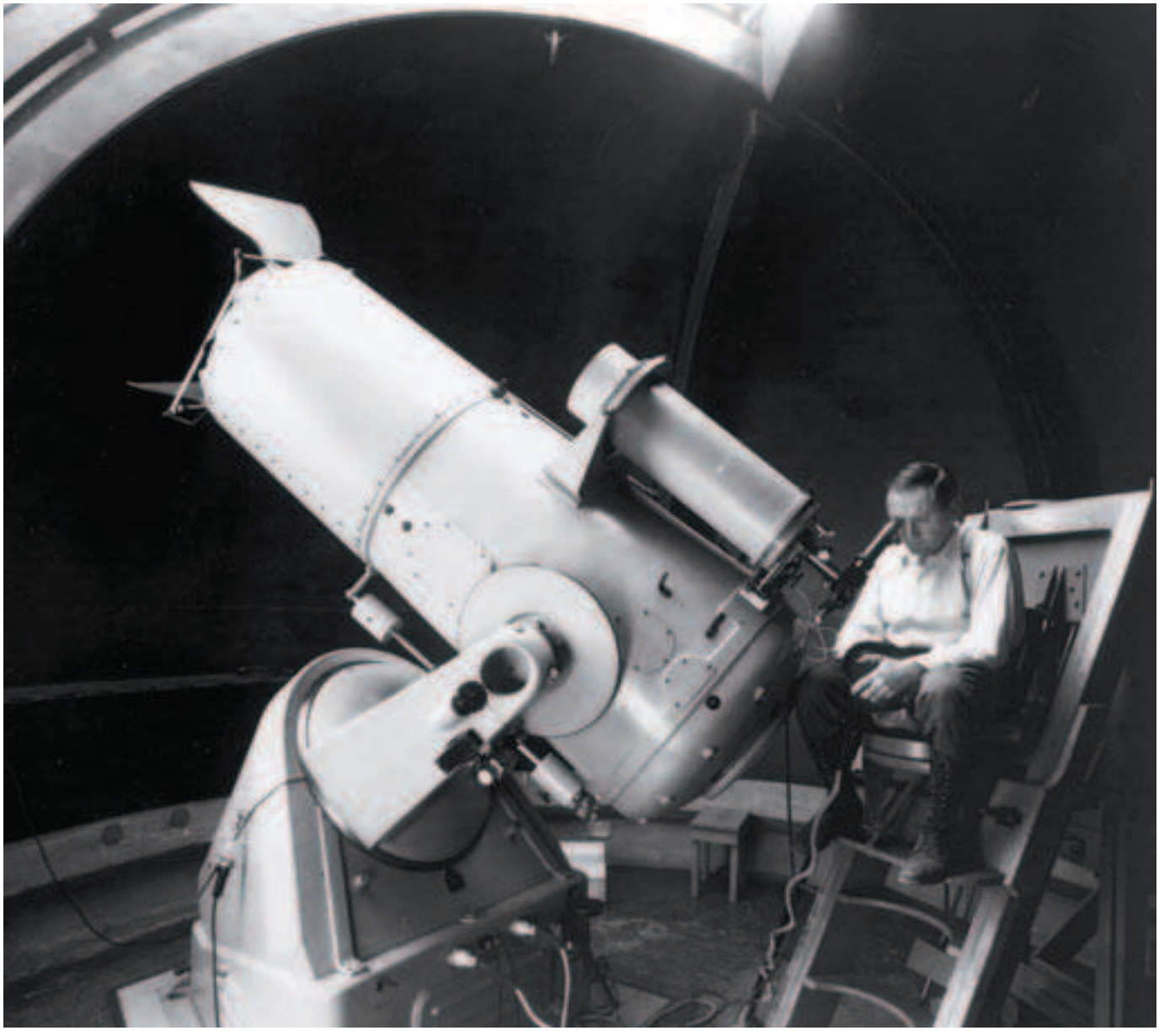
HUNT FOR DARK MATTER

No one knows for sure what makes up more than 80 percent of the matter in the universe. Though this so-called dark matter, which does not interact with light, has not been detected directly, scientists see evidence of its existence in gravitational interactions whose effects are visible in distant galaxy clusters. Now, using rapidly advancing techniques, physicists are mounting a major effort to detect the exotic particles thought to make up dark matter.

By KATHERINE BOURZAC

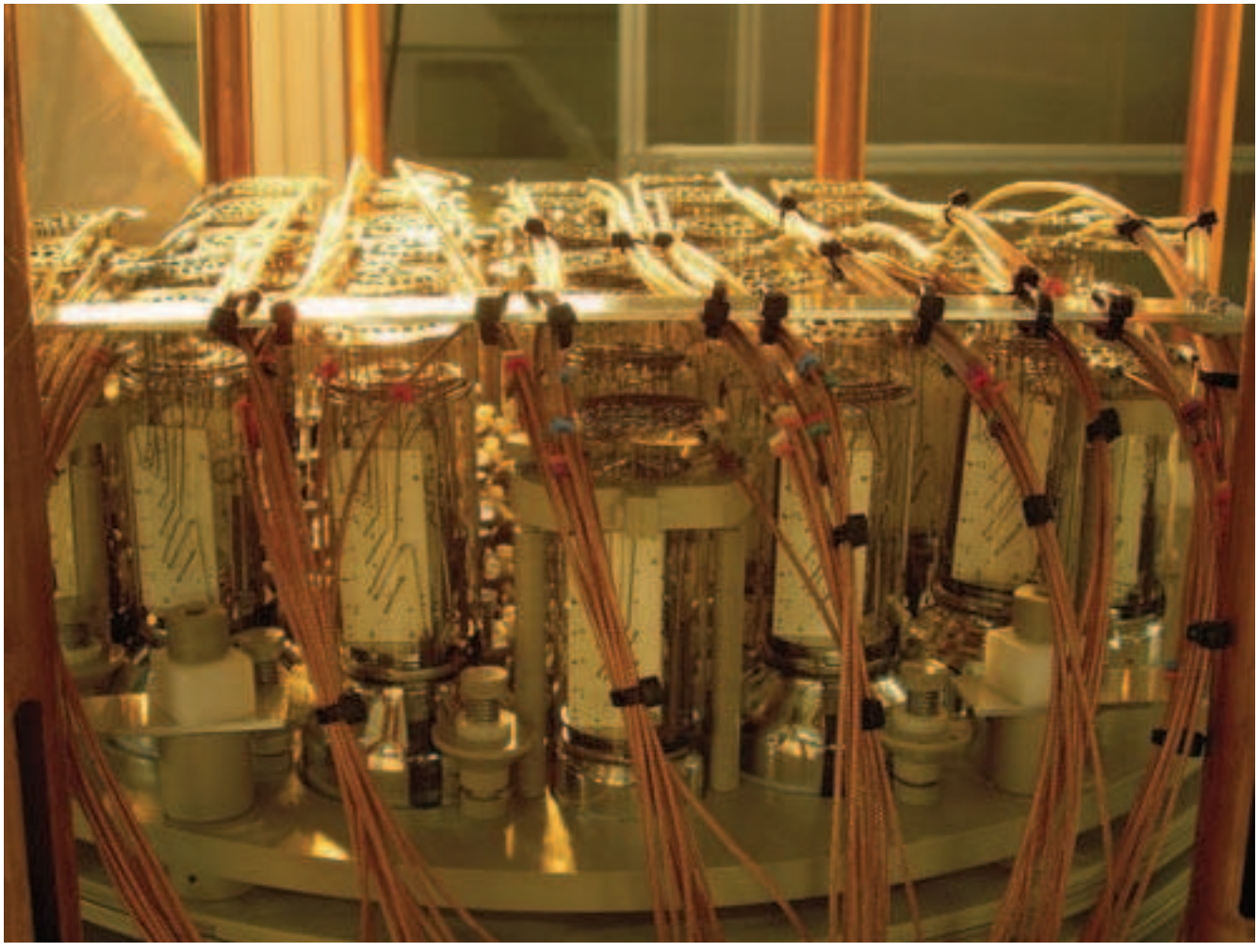
T. GREGORY GUZIK

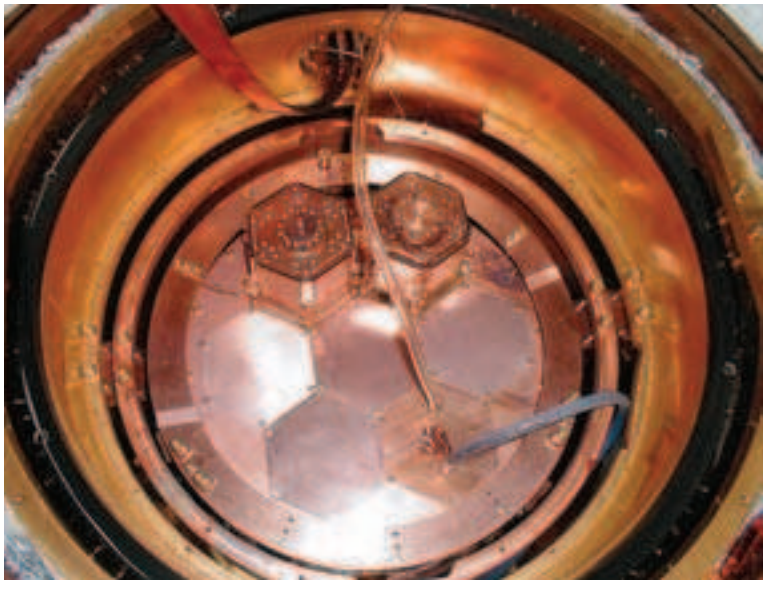
NASA, ESA, M.J. JEE AND H. FORD



Dark matter was first postulated by the Caltech astrophysicist Fritz Zwicky in papers published in the 1930s. Zwicky, shown above at the Palomar Observatory, calculated that there was more mass in a cluster of galaxies he was studying than could be accounted for by measurements from the telescopes of the day. The image on the facing page, a composite of images taken by the Hubble Space Telescope, shows how the pull of a ring of dark matter distorts the light from stars in distant galaxies.

CALTECH ARCHIVES





FRANCESCO DI POMPEO LNGS-INFN (WARP); FERMILAB (CDMS); REIDAR HAHN/FERMILAB (BUBBLE CHAMBER); ELENA APRILE (XENON)

www Hear MIT's Gabriella Sciolla talk about the hunt for dark matter: **technologyreview.com/darkmatter**

The most promising technologies in the search for dark matter are systems for direct detection of WIMPs, or weakly interacting massive particles. The detector that physicists believe is likely to find WIMPs first, called CDMS (for "cryogenic dark-matter search"), is shown at bottom left. The two hexagonal boxes contain massive semiconducting crystals held at temperatures near absolute zero. When a WIMP strikes, the nuclei of the semiconducting material will recoil in a characteristic fashion, creating an electron hole and a small amount of heat that are detected by superconducting circuits and by a film of tungsten that acts as a very sensitive thermometer. Researchers hope to see about one particle per kilogram of crystal every three months. Other WIMP detectors—including XENON, pictured above, and WARP (for "WIMP Argon Programme"), at the top of the facing page—are designed to capture nuclear recoil in vats of liquefied noble elements. The glass chamber in the center of the machine at left is filled with a liquid that will evaporate, forming bubbles as large as a millimeter in diameter, when a WIMP strikes. Because heat or cosmic rays can also cause nuclear recoil, detection will need to be confirmed by multiple technologies.

THE U.S. STIMULUS BILL INCLUDES TENS OF BILLIONS TO SUPPORT ENERGY AND INFORMATION TECHNOLOGIES. IT IS INTENDED BOTH TO CREATE JOBS IMMEDIATELY AND TO SET THE STAGE FOR LONG-TERM ECONOMIC GROWTH. SO WHY ARE ECONOMISTS AND INNOVATION EXPERTS SO SKEPTICAL?

Can Technology Save the Economy?

By DAVID ROTMAN

Part 1 of 2

By any measure, $100 billion is a staggering amount of money. That's how much the federal stimulus bill devotes to the discovery, development, and implementation of various technologies. Some $20 billion will fund the increased use of electronic medical records; another $7.2 billion will support the extension of broadband Internet access to areas currently without such services. Most impressive, roughly $60 billion will be spent on energy, funding everything from energy-efficiency programs to loan guarantees for the construction of large facilities that use new biofuel and solar technologies.

The spending is unprecedented, not only in scale, but also in the breadth of technologies it covers. For initiatives such as broadband deployment and incentives to adopt electronic medical records, the billions of dollars represent entirely new investments. And for energy technologies, the spending levels dwarf existing public and private investments. One big winner: the U.S. Department of Energy, which received $39 billion (in addition to its $25 billion annual budget). The DOE's Office of Energy Efficiency and Renewable Energy, whose budget in 2008 was $1.7 billion, alone was given $16.8 billion. By comparison, venture capitalists, who often claim clean tech as their favorite growth area, invested just $4.1 billion in that sector in 2008.

The influx of money is particularly dramatic because it comes after years of lackluster federal spending on technology and research, especially in the area of energy. The stimulus bill unabashedly singles out energy projects for huge doses of funding: $11 billion to modernize the electricity transmission system and create a smart grid, and millions to develop such new energy sources as geothermal power ($400 million) and biomass fuels ($800 million). Established renewable-energy sectors, such as wind and solar, also receive tens of billions in tax credits and grants.

Most audacious, the spending bill does all this with the intention of both stimulating the economy in the immediate future and creating growth in the long term. President Obama and others in his administration have repeatedly connected the stimulus spending with the need to begin creating "green jobs" and building a "clean-energy economy."

The decision to make large energy investments in hopes of realizing both immediate economic benefits and longer-term environmental dividends represents a "massive shift" in government policy, says Robert Pollin, a professor of economics at the University of Massachusetts, Amherst. Pollin published a report last fall arguing that substantial spending on energy technologies would create two million jobs over the next two years. The idea that spending on energy technologies to address global warming

could have an immediate economic benefit, he says, "would have been considered preposterous less than two years ago." Yet his study now reads like a blueprint for much of the stimulus bill's energy funding.

But just how realistic are the expectations behind the stimulus package? Can huge jumps in technology funding boost the economy? And will this sudden windfall of funding really be a positive force in encouraging new technologies?

Almost all economists agree that technological progress drives long-term economic growth. Many proponents of the technology provisions in the stimulus bill go further, however, arguing that the funding will also create jobs immediately. Daniel Kammen, founding director of the Renewable and Appropriate Energy Laboratory at the University of California, Berkeley, estimates that investments in renewable energy create three to five times as many jobs as the equivalent investments in fossil-fuel energies. "Energy efficiency and solar, in particular, have been shown to be two of the highest job-creating industries that we know," he says.

> The concern over the stimulus bill's technology spending is not just that it offends conventional macroeconomic theory about the best way to boost the economy; it's that it might harm the very technologies it means to support.

And he believes there is clear evidence that spending on energy research will improve the performance and reduce the cost of renewable technologies already on the market.

But a number of economists and policy experts who think about these issues regard the stimulus package's technology funding with ambivalence or even dismay. They worry that the bill conflates the challenges of immediate economic stimulus and long-term technological progress, particularly in the area of energy. Thus, they say, it may not be the most effective way to achieve either goal.

In macroeconomic theory, a stimulus package has a clear, simple function: during economic slowdowns, governments increase their own spending to compensate for the fact that consumers and businesses are spending less. "A stimulus is a sudden and dramatic intervention into the economy," says Robert Stavins, director of the Harvard Environmental Economics Program. And the key to its effectiveness is that it is labor intensive and quick. While some projects to make buildings more energy efficient might qualify as a short-term boon for the economy, Stavins says, other energy-related projects, like rebuilding the electricity grid, will take years and have little immediate effect. "Greening the infrastructure is highly desirable, but it is not going to happen quickly," he says.

The concern over the stimulus bill's technology spending is not just that it offends conventional macroeconomic theory about the best way to boost the economy; it's that it might harm the very technologies it means to support. Because the bill was written quickly and shaped by political expediency, economists and experts on innovation policy are leery of many of its funding choices. Could extending billions of dollars' worth of fiber-optic lines to rural communities, for example, become a boondoggle? Or what if utilities run high-power transmission lines to remote solar or wind farms, only to find that the electricity they produce is too expensive to compete with other sources ?

As a historical analogy, experts point to corn-derived ethanol. Once the darling of alternative-energy advocates, the heavily subsidized biofuel is now routinely condemned by both environmentalists and economists. Yet because ethanol's use in gasoline is now mandated by federal law, and a large industry is now invested in its production, its production is likely to continue even though it offers few environmental benefits over gasoline.

The problem with the stimulus package is that it is "very much a heterogeneous bag of things," says Daron Acemoglu, an economist at MIT and an expert on the role of technology in economic growth. "It's very much like pork-barrel politics," he says. As a result, it's hard to properly evaluate the different spending programs. And, he suggests, "when you make investments in bad projects under the name of stimulus and in the name of technological investments, you're doing damage in a number of ways. First of all, you're not helping; second, you're confusing matters; and third, you're poisoning the well for the future."

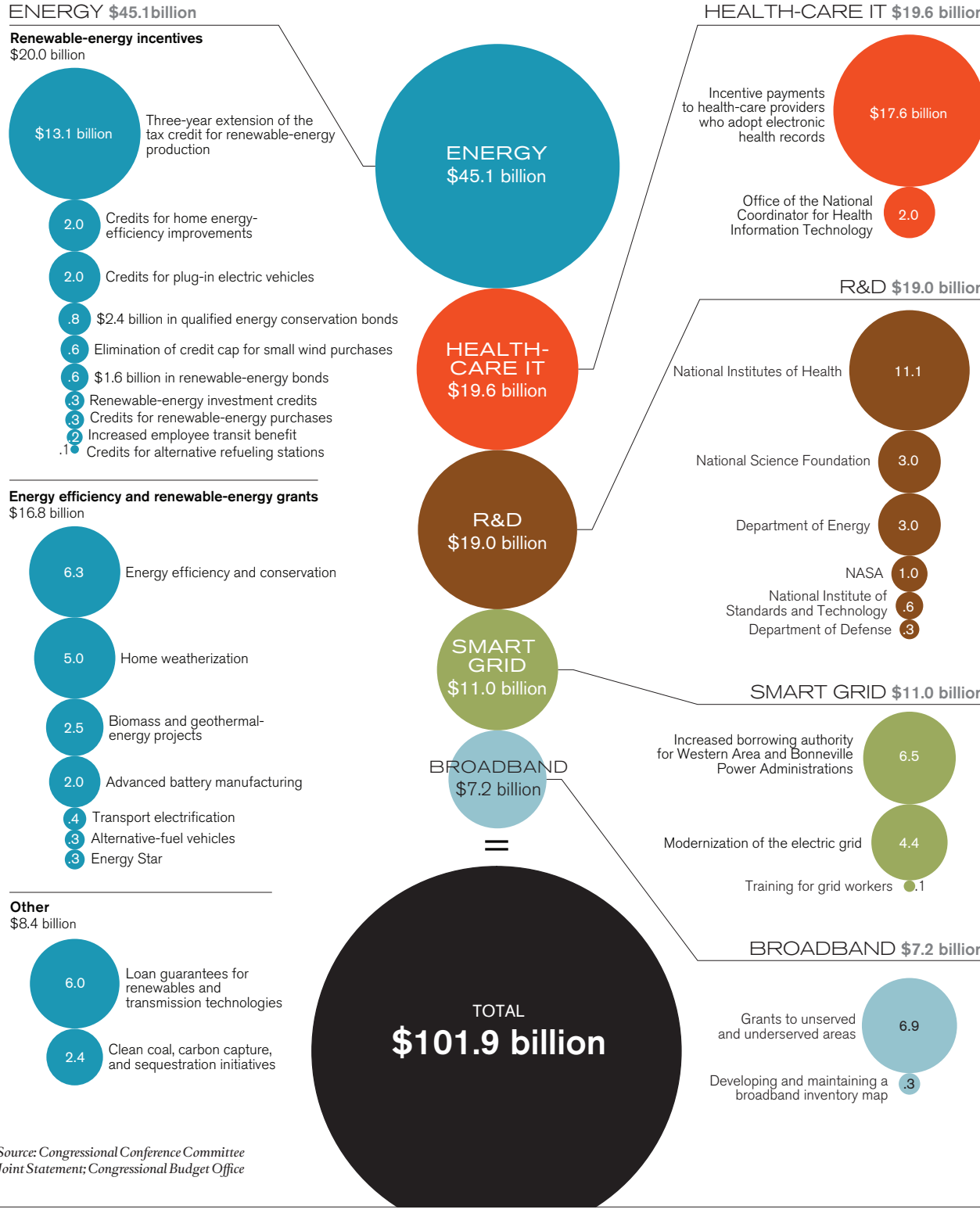
SOLAR BOTTLES

Less than a week after the passage of the stimulus bill, Robert Atkinson is taking stock of the legislation. Maybe it's the early hour or the freezing weather that still grips Washington, DC, in late February, but the president of the Information Technology and Innovation Foundation (ITIF), a nonprofit think tank that argues for federal policies to promote technology, doesn't seem in a celebratory mood. Despite what would seem to be a huge victory for his cause, he still seems irritated by the bickering over the details of the stimulus package.

Much of the bill's spending plan is strikingly similar to proposals that his own group has presented. In a report published in

WHO GETS WHAT

Breakdown of technology, energy, and R&D spending in the $787 billion economic-stimulus act signed into law February 17, 2009



Source: Congressional Conference Committee Joint Statement; Congressional Budget Office

TOMMY McCALL

January, the ITIF estimated that roughly a million jobs would be created by spending $30 billion on broadband, smart-grid technology, and health-care information technology in 2009. While the stimulus bill broke down the spending slightly differently and extended it over several years, such forecasts of job creation served to justify the inclusion of heavy technology spending in the legislation.

Likewise, a study prepared last fall by UMass's Pollin and his colleagues shows how spending $100 billion over the next two years on energy-related investments could create two million "green" jobs. The report identified six funding areas, including solar, wind, and advanced biofuels, that it argued would create jobs and facilitate transition to a "low-carbon economy." Although Pollin says he researched and wrote the paper as an academic, the work was published in September by the Center for American Progress, a think tank whose CEO, John Podesta, led Obama's transition team. And like the ITIF study, Pollin's report foreshadowed many of the spending provisions in the stimulus legislation. Pollin notes that while the bill's spending for energy conservation and renewable energy is lower than the total recommended in his report, many of the legislation's details "are kind of what I proposed."

The theoretical justification for the government's stimulus package derives from John Maynard Keynes, the 20th-century British economist. Writing during the height of the Great Depression, Keynes famously suggested that if better job-creation schemes were not available, the British Treasury should fill bottles with money and bury them in old coal mines for people to dig up. That idea is central to the ITIF's policy suggestions, Atkinson says: "Our main message is that innovation could be Keynesian in nature. In other words, solar-energy bottles."

Atkinson has little patience with critics who object that investing in long-term technology growth requires a more deliberate strategy; they are "being naïve to the real world," he maintains. "This is our one chance," he says of the massive infusion of government funding for new technologies. "It's almost like free money." Those who criticized the bill's provisions for technology spending didn't understand that innovation could have a big short-term stimulus effect and, at the same time, "have a much better long-term effect than virtually anything else in the package," he says. "They couldn't walk and chew gum at the same time."

Indeed, that deliberate mixing of two goals—immediate job creation and economic growth through the development of IT and energy technologies—is just what rankles many economists. Paul Romer, an economist at the Stanford Institute for Economic Policy Research, is one. "If I sat down and tried to design a stimulus bill most likely to be effective to getting us back to full employment, there is a good chance that this kind of spending on technology would not have been a part of that bill," says Romer, who has spent his career studying the relationship between technological progress and economic growth. The prospect of spending so much money on technology projects and science programs provoked a "feeding frenzy," he says. "Everyone was trying to grab as much as they can."

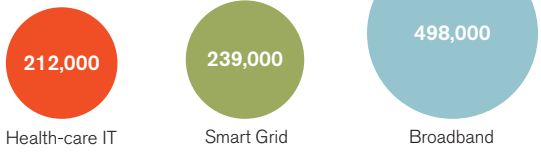
"If we believe subsidies will speed up technological change, we should do that on its own terms, separate from a stimulus," says Romer. And he worries that the heavy technology spending in the bill could eventually deter innovation strategies that would prove more effective. "The cost here is not only the dollars," he says. "[It] may also be the dog that doesn't bark—the truly important program that we could have put in place if we went about encouraging innovation in a thoughtful way. Having prominent

THE JOBS JOLT

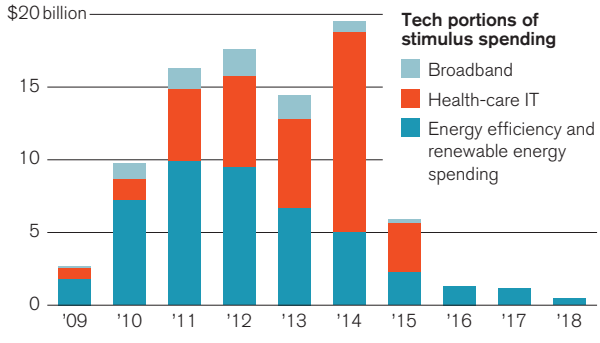
According to the administration's economic analysis, the stimulus bill will result in more than three million jobs over the next two years. Last year, the Information Technology and Innovation Foundation predicted that a $30 billion investment in digital infrastructure would mean nearly a million jobs. Its analysis assumed that the money would be paid out over a year (for the smart grid, the estimated spending was $50 billion over five years), but a report from the Congressional Budget Office estimates that much of the technology spending will not reach the economy until 2012 or later.

JOBS WILL BE CREATED ...

Estimate of jobs created or retained per $10 billion invested



... BUT IT WILL TAKE TIME FOR THE STIMULUS MONEY TO BE SPENT.



Source: Information Technology and Innovation Foundation; Congressional Budget Office

TOMMY McCALL

failures can undermine the whole case for using resources wisely to encourage innovation."

BROADBAND BOONDOGGLE?

One area of technology spending in the stimulus package that appears to flunk economic analysis is the program to extend broadband Internet to areas not currently served. Broadband has already been built out to the areas where it makes economic sense, says Shane Greenstein, a professor at Northwestern University's Kellogg School of Management. "If there was money to be made, someone did it," he says. "It's 2009, not 2003."

According to a recent survey by the Internet and American Life Project of the Pew Research Center, a nonpartisan organization based in Washington, DC, less than half the adults in the United States lack broadband service. Most of those people say they don't want it, either because it is too expensive or because they're just not interested. Only 4.5 percent of U.S. households (roughly 5.2 million) say they want broadband access but don't have it. The problem, says Greenstein, is that these households tend to be in isolated or rural areas where supplying broadband is extremely expensive. Whereas it costs approximately $150 to bring the service to an urban household and $250 to bring it to a suburban one, he says, no one really knows how much it will take to bring it to areas not currently served, since the costs for different residences will vary widely. The most optimistic estimate is that it will cost at least a thousand dollars per household to extend broadband coverage; for some isolated houses, the cost will be far greater. Even in the best-case scenario, Greenstein says, the stimulus package won't extend service to many who want it. "It easily falls short," he says. "And if it is even more expensive per household [than a thousand dollars], the money goes really fast and doesn't accomplish much."

What's more, says Greenstein, the benefit to local economies will be limited. His analysis shows that the largest financial gain from expanding broadband access goes to broadband suppliers themselves. Increasing broadband use can also benefit equipment makers and companies such as Google and Amazon, he says. The advantage that households would gain in switching from dial-up access to broadband is hard to quantify, but it "can't be big," he says. "I'm skeptical there are many local benefits from this." What is clear, according to Greenstein, is that any benefits add up to far less than the hundreds of billions of dollars that have been cited by Washington advocates of the stimulus spending.

Of course, advocates of federal spending to extend broadband service argue that it provides more general benefits to society. Remote communities would gain increased educational opportunities, easier access to government services, and eventually, perhaps, improved medical treatment through online interaction with physicians. But, says Greenstein, many of these benefits are several years away, and it is debatable whether expanding conventional broadband services—rather than, say, using wireless technologies—is the most effective way to deliver them. What's more, he adds, the $7 billion expenditure in the stimulus bill seems arbitrary. "How they got that number is a puzzle to me," he says. "Why not $15 billion? Or $3 billion?"

WHAT GREEN ECONOMY?

Innovation in science and technology is estimated to account for as much as 90 percent of new economic growth. The reason is that better technology allows more things to be produced more cheaply and can create entirely new markets; in the terminology of economists, it increases productivity. For economists, the most dramatic recent example is the information technology boom that began in the mid-1990s.

Beginning in 1995, productivity began to grow at a much faster rate than it had in years. (While strong productivity growth in

the decades after World War II fueled the prosperity of that era, it fell off abruptly in the mid-1970s, contributing to an economic slowdown.) The jump first seen in 1995 was initially viewed as an anomaly, but productivity continued to rise over the next several years. As economists scrambled to figure out why, entrepreneurs raced to take advantage of the "new economy."

Though it took economists several years to figure out exactly what was driving the bump in productivity, Dale Jorgenson, a professor of economics at Harvard and former president of the American Economic Association, says it is now clear that the decreasing cost of computer hardware and software dramatically increased the role of information technology in the economy during the 1990s. Even though IT spending represented only about 3 percent of GDP, it was having "a tremendous impact," says Jorgenson: "IT probably accounts for almost all the growth in productivity in the boom of the 1990s, and it is still perking right along."

Could the green economy be the *new* new economy, with energy technologies replicating the success of information technologies in boosting productivity? Jorgenson is skeptical. In fact, he says, today's scenario is the "extreme opposite" of the one in which market demand drove the use and implementation of information technology in the 1990s. "A lot of these [energy] technologies that are going to be subsidized are not commercially viable without a subsidy," he says. "These things have been around for a quite a while, and have never gotten to the stage of being financially viable without sizeable subsidies. What does a subsidy mean? It means it's not good for the economy. It doesn't meet the market test, so there has to be some other reason to do it."

Of course, the other reason for investing in new energy technologies is to address climate change. But Jorgenson says the best way to encourage innovation for that purpose is through carbon pricing—either a direct carbon tax, which he advocates, or the cap-and-trade program that is now being debated in Congress. Such a market-based program would produce "a shift to noncarbon technologies," says Jorgenson. Meanwhile, if there is going to be a carbon pricing program in the near future, he says, it "doesn't really make a lot of sense to be funding energy stuff" in the stimulus bill. It will be less risky, he says, to let the carbon pricing scheme determine which of the renewable-energy technologies are viable in the market.

MIT's Acemoglu agrees. While he is optimistic that energy technologies will be "a great platform for economic growth" and can eventually play the same type of role that hardware and software did in boosting the economy, he too is skeptical of the subsidies in the stimulus bill. "I'm quite confident that alternative energies, new hybrid vehicles, new power sources, a more sophisticated power grid, will be one of the handful of sectors that will spearhead the growth of the economy over the next decade," says Acemoglu. But, he adds, "a lot of that [growth] will be market generated."

Instead of providing subsidies to develop new technologies, says Acemoglu, the government should establish a carbon tax and support research. The federal government, he points out, played a critical role in the development of IT by supporting the early, basic research that led to the Web and by funding research programs in computer science and electrical engineering. But it would have been "a kiss of death," he says, if the government had tried to dictate how to wire computers or define the type of software that should be used.

Likewise, the government should encourage the development of new energy technologies by supporting research, says Acemoglu, but "more soberly" than it does in the stimulus bill. He suggests "limited but well-designed funding for the National Science Foundation and other agencies that will create the right type of synergies between private, public, and university research." That, he says, would create an environment conducive to energy R&D.

BECALMED

While academic economists might be worried about long-term growth strategies, the entrepreneurs and executives running renewable-energy businesses, including solar, wind, and biofuel companies, say they are struggling just to stay alive. The credit and banking crisis that took hold last fall ruined any chance of obtaining financing for most large-scale, capital-intensive projects. As a result, construction on many costly solar-power and wind-energy facilities came to a halt, and a number of companies announced layoffs. Those developing truly novel technologies, such as cellulosic biofuels, were left stranded without the prospect of obtaining the hundreds of millions in private financing needed to demonstrate their technologies on a larger scale.

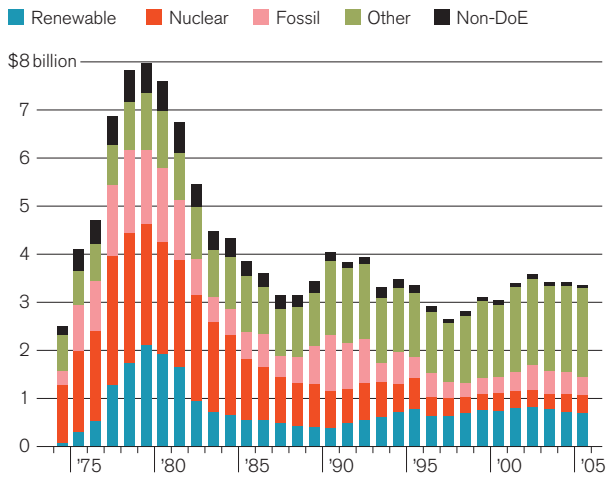
"It is really ugly out there for a lot of these technologies," says David Victor, director of the Program on Energy and Sustainable Development at Stanford University. One of the biggest potential benefits of the stimulus bill is that it might well "protect the [renewable-energy] sector in a period when it would otherwise be absolutely pummeled by market forces," he says. "If the sector were to blow up, it would take a while for people to put Humpty Dumpty back together. And during that period, a lot of these companies would just disappear completely."

The cellulosic-biofuels sector, in particular, is at a crossroads, says Bruce Jamerson, chairman and CEO of Mascoma, a Boston-based startup specializing in advanced biofuels. Though often touted as a source of alternative transportation fuel that doesn't have the environmental drawbacks associated with corn-based ethanol, cellulosic biofuels are not yet produced commercially in the United States, because they are too expensive. Mascoma wants to construct a commercial-scale facility in northern Michigan that could be in operation by 2012, says Jamerson. But building the plant will cost from $300 million to $325 million. Without

ENERGY R&D SLOWDOWN

The stimulus bill will boost public-sector spending on energy research and development, which has been on the decline for decades.

ENERGY R&D BY TECHNOLOGY
(in 2002 dollars)



Source: G.F. Nemet and D.M. Kammen (2007), "U.S. Energy Research and Development: Declining Investment, Increasing Need, and the Feasibility of Expansion."

the grants and loan guarantees in the stimulus package, he says, "it would be very difficult to get a deal done with large equity investors and lenders on a commercial plant."

A slew of provisions in the stimulus legislation will indeed benefit these fledgling clean-energy businesses. Howard Berke, executive chairman and cofounder of Konarka, a manufacturer of organic photovoltaics based in Lowell, MA, says that 17 provisions will "in one form or another" benefit the solar industry; they include a refundable tax credit that will effectively cover 30 percent of the cost of solar projects, a $6 billion loan guarantee program for renewable projects, and investment credits for manufacturing facilities built in the United States. The Solar Energy Industries Association estimates that overall, the provisions will create 110,000 jobs over the next two years.

Beyond helping companies in the energy sector survive the recession, the stimulus bill could—supporters hope—jump-start fledging technology sectors such as the smart grid, the effort to modernize the electricity infrastructure so that energy can be distributed more cost-effectively and used more efficiently. Federal spending on an improved power grid could, in turn, increase industry's spending on electric vehicles and renewable power, advocates argue. And it will begin to spur further investments in improving the electric grid. The $4.5 billion that the legislation devotes to smart-grid technology is barely enough for one utility to build up its transmission system, says Martin Fleming, IBM's vice president of corporate strategy. However, he says, by "providing incentives for the progress to begin," the bill could give smart-grid technology the market momentum it needs to survive when the incentives go away.

Indeed, what happens when the stimulus spending ends will largely determine the bill's real impact on technology. The danger, of course, is that while the federal dollars could help renewable-energy companies survive the recession, they could also prop up existing technologies that would not be competitive in an open market. Not only could the federal spending support uneconomical energy sources (as has been the case with ethanol), but the resulting backlash could discourage policy makers, investors, and the public from embracing newer, more efficient technologies. As the stimulus runs its course in two to three years, pressure to reduce the federal budget and cut government spending could make such a backlash even worse.

One renewable sector that could be particularly vulnerable in such a scenario is the solar industry. Photovoltaics "still have a way to go on the learning curve," says Henry Lee, director of the Environment and Natural Resources Program at Harvard's Belfer Center for Science and International Affairs. Not only are they still too expensive, but researchers need to develop longer-lasting, more efficient solar cells that can handle higher voltages. Though Lee is encouraged by the stimulus bill's emphasis on solar and wind energy, he fears that by funding the construction of extensive solar capacity using existing photovoltaic technology, it could distract attention from the effort to improve renewables. "What you want to stimulate is learning to build better wind turbines and solar collectors," says Lee. Instead, he says, much of the funding is focused on "how many windmills and solar panels you can erect."

GREAT EXPECTATIONS

By the end of this year, Congress is likely to debate—and perhaps pass—ambitious legislation that will, like the stimulus package, help redefine the economics of energy technology for decades to come. While the specifics are still being considered, the legislation is likely to introduce a cap-and-trade program to set pricing for carbon-based energy sources, establish nationwide standards for renewable electricity, and provide provisions to modernize long-distance electricity transmission systems. In such a context, the stimulus bill is just one part of a larger energy agenda that will, arguably, be the most important change in technology policy for a generation.

Such laws could help address global warming. But few energy experts believe that renewable technologies will be reliable and cheap enough to replace fossil fuels on a large scale anytime soon. Electricity produced by existing solar technologies is likely to

TOMMY McCALL

remain relatively expensive. Advanced biofuels are also too expensive, and they're years away from significantly cutting into gasoline consumption. Overhauling the electricity grid will take years, cost at least a hundred billion dollars, and require new storage technologies in order to be fully effective. In testimony before Congress this March, Secretary of Energy Steven Chu stressed the importance of finding "transformational technologies" in all these areas. He noted, among other things, the need for "photovoltaic solar power that is five times cheaper than today's technology."

No doubt, then, new funding for research will be critical to the search for low-carbon technologies. Somewhat overshadowed in the stimulus bill is the $1.6 billion increase for basic science at the DOE. Even more encouraging, the legislation included $400 million to start up and fund the Advanced Research Projects Agency–Energy (ARPA-E), an office designed to mimic the success of the original ARPA program that pioneered such breakthroughs in information technology as the precursor to the Internet. Programs like ARPA-E, which emphasizes government and industry research on high-risk programs, are likely to yield significant advances. It's also encouraging that in his recent 10-year budget plan, President Obama proposed almost $75 billion for a permanent R&D tax credit to stimulate private funding of research.

The money is welcome to many in the research community, especially after years of declining federal and private support *(see "Energy R&D Slowdown," p. 51)*. But the new emphasis on energy R&D is also a stark reminder that, almost 30 years after such funding peaked in the late 1970s, there are still no good or easy answers when it comes to replacing fossil fuels. Recent statistics from the DOE's Energy Information Administration reflect the lack of progress: coal-fired power plants still supply the overwhelming bulk of the nation's electricity, while solar, wind, and geothermal together provide about 2 percent (and most of that comes from wind power). There is little, if any, sign that the green economy has even begun to sprout.

Congress and the president were, arguably, right to attempt to revitalize energy research and to link technology spending to the long-term objective of transforming the country to a clean-energy economy. Including R&D and other technology programs in the stimulus bill makes evident to the public what every economist knows: long-term economic growth depends on innovation and technological progress. Most important, it has once again established energy research and the search for cleaner power as a national priority.

But including so much technology spending in the stimulus bill also brings dangers. Technology—more specifically, technological progress—can save the economy. A cleaner energy infrastructure will prove invaluable to economic growth in the long term. However, it will take time to realize the benefits. By confusing immediate help for the economy with technology's role in creating growth, the stimulus bill runs the risk of raising unrealistic expectations that could backfire in the face of inevitably slow progress.

If the transition to a clean-tech economy is ever truly to begin, government policy makers will have to move past politics and get the economics, policy, and technologies right. The way technologies are chosen, implemented, and funded will matter. That means properly designing a carbon pricing program and supporting institutions like the DOE in the expectation that they will make informed decisions and work closely with private investors and venture capitalists to develop the most viable technologies. Perhaps most important, it means that the government will need to support and fund energy research even as the stimulus spending peters out and political support for massive technology funding wanes.

Richard Lester, director of MIT's Industrial Performance Center and a professor of nuclear science and engineering, seems clearly ambivalent about the merits of the technology funding in the stimulus bill. "Would it be better not to spend the money on R&D? Probably not," he says, choosing his words carefully. "I just don't think we should have high expectations." The difficulty, he says, will be to select the right research projects, given the sudden flood of money. "It would be prudent to expect that a lot of the money will not be well spent," he says.

The stimulus bill makes evident to the public what every economist knows: long-term economic growth depends on innovation and technological progress. But including so much technology spending in the legislation also brings dangers.

Adds Lester: "I don't think there is an understanding of the scale of the task that lies ahead. This will be a long transformation, and it is going to be very expensive." The reinvention of the nation's energy sources, he says, "is inherently a project on the time scale of several decades." TR

Part II will take a look at how the stimulus money is being spent around the country.

DAVID ROTMAN IS THE EDITOR OF *TECHNOLOGY REVIEW*.

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Manipulating Memory

DRUGS THAT ALTER TRAUMATIC RECOLLECTIONS OFFER NEW HOPE FOR TREATING ANXIETY DISORDERS. THEY COULD ALSO CHANGE THE WAY WE THINK ABOUT MEMORY.

By EMILY SINGER

For psychologist Alain Brunet, the case is still astonishing. When Patrick Moreau first came into his office suffering from post-traumatic stress disorder (PTSD), the Canadian soldier, who had served as a United Nations peacekeeper in Bosnia, could hardly bear to recount the details of the day he was taken hostage in 1993. The memory—of kneeling on the ground with his hands on his head, legs shaking, a stark line of trees across the sky—aroused crippling fear that felt as fresh as it had 15 years before. The glimpse of a particular tree line through his windshield was enough to bring the memory rushing back, giving him such violent shakes that he would have to pull off the road.

But six months after participating in Brunet's clinical trial, Moreau no longer meets the diagnostic criteria for PTSD. He still experiences some flashbacks, but they are less frequent and less intense. He can now talk calmly and openly about what happened. And all he did was take a blood-pressure drug after writing down the details of the traumatic experience.

"It seemed like science fiction," says Brunet, a clinical psychologist at McGill University and the Douglas Institute in Montreal. "If someone is traumatized, you ask them to recall the memory, give them a pill, and the [emotional] strength of the memory is weakened." The details of the trauma remain intact, but the emotional component of the memory appears to dissipate. Although larger studies are needed to assess the potential benefits of the treatment, preliminary findings are promising. Brunet has successfully treated PTSD not only in soldiers like Moreau but also in survivors of rapes and car accidents. "They are matter-of-fact," he says. "When we ask them whether they have been thinking about the trauma, they raise their shoulders and say, 'Eh, I am not thinking about it so much.' It's like it's no longer an issue."

Brunet's potentially transformative treatment is based in part on a surprising experimental observation: the simple act of calling a memory to mind makes it vulnerable to alteration. Indeed, the right drug given at the right time can make parts of it disappear altogether. If different drugs are delivered to specific parts of the brain, lab animals will explore cages they've been conditioned to fear, drink fluids once associated with certain sickness, and ignore sights and sounds that previously led them to expect cocaine or other pleasure-inducing drugs. Humans, too, can be tricked into scrambling their memories in specific ways. For example, if people learn a list of words soon after recalling a previously learned list, they tend to forget the old list or incorporate those words into the new one. The memory of the old list remains intact if people aren't reminded of it just before learning the new one. And it's always the old list that gets incorporated into the new, not the other way around.

Brunet and others believe that this phenomenon has to do with a process called memory reconsolidation. The idea is that after someone calls up a memory, it has to be stored in the brain anew. During this process, the memory is in a changeable state. The concept of reconsolidation is still controversial among neuroscientists. But if the theory is correct, and if researchers can figure out just what happens to brain cells and the connections between them when a memory is recalled, it could help answer one of the biggest questions in neuroscience: how memories are physically saved and updated in the brain. It could also explain the malleable nature of memory. "It gives us a new perception of a component of memory we didn't understand before—how the imperfectness of recall may come about," says Eric Kandel, a neuroscientist at Columbia University and winner of the 2000 Nobel Prize in medicine.

Illustration by GÉRARD DUBOIS

Brunet is one of the few people studying reconsolidation in humans. In his trials, he administers a medicine called propranolol, which is already used to treat high blood pressure. It decreases blood pressure by blocking the action of epinephrine, a stress hormone, in the peripheral nervous system. But it also blocks the hormone in the amygdala, a part of the brain that plays a crucial role in storing the emotional components of memory. If Brunet proves that this treatment can weaken the grip of painful memories, he won't just have found an alternative to behavioral therapy and existing drug treatments for PTSD, none of which work for everyone. He will also have demonstrated that it might be possible, through drug treatment, to fundamentally and precisely alter memories beyond the confines of the lab. The implications are immense. Brunet's general approach to understanding memory could be used to treat a variety of anxiety disorders and addictions.

A WINDOW OF VULNERABILITY

At the simplest level, a memory is thought to be stored in the brain by a specific, well-connected circuit of nerve cells linked by junctions called synapses. New memories are formed when synapses form or existing synapses grow stronger as the brain processes events.

One of the tenets of modern neuroscience is that it takes time for these memories to become permanent—a process dubbed consolidation. In the 1960s, scientists subjected rats to various treatments that block normal brain signaling (for example, electroconvulsive treatment, or ECS, disrupts electrical signals by inducing seizures). The results showed that very new memories could easily be kept out of permanent storage. But if the disruptive treatments were administered a day or so after the new memory was created, they had no effect. Once a particular memory becomes resistant to interference, it is regarded as consolidated.

The first hint that long-term memories could be made malleable came in the 1960s too, just as the idea of consolidation was gaining ground. Through experiments similar to those that defined the time window for consolidation, scientists discovered that ECS could disrupt even an old memory in animals, if the animal was reminded of it first. To start, the researchers would condition rats to fear a particular sound by giving them a mildly painful shock every time they heard it. The animals would eventually freeze in fright on hearing the sound: the painful memory had been consolidated. But when the rats were given ECS treatment just after the memory was triggered by playing the sound, the fearful link between the sound and the shock was lost forever. Because this rather confusing finding conflicted with the dominant theory that consolidated memories are permanent, it was pursued only briefly, and then largely forgotten for the next 25 years.

Over the next few decades, scientists came up with more precise ways to study the molecular underpinnings of memory and consolidation. In 1999, for example, researchers in neuroscientist Joseph LeDoux's lab at New York University found that injecting a drug that blocks protein synthesis directly into part of the brain disrupted consolidation of new memories. Researchers proposed that when the right proteins aren't produced, nerve cells can't make the connections that underlie memory formation at a cellular level.

In 2000, Karim Nader, then a postdoctoral researcher in LeDoux's lab (he is now an associate professor at McGill), published a paper showing evidence that the same drug treatment could also erase long-term memories that had recently been recalled—a major new challenge to the prevailing views about consolidation. Nader, who was new to memory research but had access to neuroscience not available in the 1960s, outlined a specific theory explaining this observation. He proposed that recalling a memory actually causes the synapses encoding that memory to weaken or even to come apart. The molecular structure of the memory—the series of synapses in which it's stored—is then re-formed, or reconsolidated, to make it stable once again.

When Nader presented his work in 2001 to a crowded lecture hall at the annual meeting of the Society for Neuroscience, the field's premier academic gathering, he faced outright disbelief from some leaders in the field. "It caught the attention of lots of other neuroscientists, because some had taken the view that once consolidation had been completed, it couldn't be dislodged," says David Riccio, an experimental psychologist at Kent State University in Ohio, whose own research in the 1970s had challenged the consolidation model.

It makes sense that the brain, in order to take in and store new information, would need to have some flexibility in the way it stores old memories. But does this really mean that when an old memory is recalled, the brain must dismantle the synaptic structure underlying the memory and then form it again? "Reconsolidation strikes me as a woefully inefficient way to make memory work," says Ralph Miller, a behavioral neuroscientist at the State University of New York at Binghamton, who was also involved in the 1960s consolidation debate. "My own best guess is that every time we recall a memory, we lay down new versions." In this model, the existing memories would remain intact, but they would be integrated with the new ones or superseded by them—meaning that the old memories would still exist in the brain but would be less accessible than the new ones.

Despite such doubts, evidence for the theory of reconsolidation is piling up. One experiment, for example, has found that blocking the molecules involved in protein degradation, which is necessary to break down synapses, makes animals forget a memory after it's been recalled. The finding suggests that reconsolidation—which couldn't happen without the initial breakdown—is the only way to explain why such memories don't normally vanish.

A more recent experiment, published late last year, begins to get at the purpose of reconsolidation: it may help update memories, integrating them with information about related newer

It makes sense that the brain would need to have some flexibility in the way it stores old memories. But does this really mean that when an old memory is recalled, the brain must dismantle the synaptic structure underlying the memory and then form it again?

experiences. Jonathan Lee, a neuroscientist at the University of Birmingham in the United Kingdom, trained rats to fear a certain chamber by shocking them soon after they entered it. More training strengthened the association; evoking the memory made these rats freeze for longer than rats trained over just one day. Then Lee blocked a protein required for the consolidation of new memories; in a second set of animals, he instead blocked a gene that is critical to reconsolidation. He found that blocking consolidation did not interfere with the strengthening of the memory, while blocking reconsolidation did. This suggests that reconsolidation, not consolidation, is what's important in strengthening memories, which is one way of updating them. "Learning something for the second time seems to use the reconsolidation mechanism," says Lee. "Learning is strengthened by going back to the initial memory."

Lee's work implies that new versions of a memory are not laid down on top of a surviving old version when the memory is updated, as Miller's alternative explanation suggests. Rather, the instability of a recalled memory may be crucial to the updating process. "Our assumption is that when you activate a memory, you set it up to be updated," says Lynn Nadel, a neuroscientist at the University of Arizona. "You make [the memory] fragile so that it is open to being changed."

Still, many questions about reconsolidation remain. Several experiments have shown that under some circumstances, erased memories can come back, suggesting that the initial memory was not truly erased. Meanwhile, both the age of the memory and its initial strength sometimes seem to affect how malleable it is: older memories, for example, can be more resistant to alteration, though that's not always the case. Some scientists see these limitations as evidence that Nader's theory of reconsolidation doesn't adequately explain recall-induced forgetting. But it may be that reconsolidation happens only under specific conditions or with specific types of memory, while other mechanisms are used to update memory in the other situations. What we don't yet understand is which types of memory are vulnerable to alteration and under what circumstances, says Jerry Rudy, a neuroscientist at the University of Colorado in Boulder, the author of *The Neurobiology of Learning and Memory*. Other researchers are now exploring whether reconsolidation is a fairly limited occurrence or one that's fundamental to memory as we conceive of it.

Even as the evidence for reconsolidation accumulates, the idea that the neural connections underlying our memories routinely come undone has some disturbing implications. Among the most significant is that our memories are vulnerable to inadvertent alteration. If the brain went to the trouble of storing a memory, why would it then have a mechanism that makes it so easy to erase? "It just doesn't make sense that a cherished childhood memory should become vulnerable to erasure," says Larry Squire, a neuroscientist at the University of California, San Diego. That vulnerability also has positive implications, however: the potential to weaken bad memories.

PAINFUL PASTS

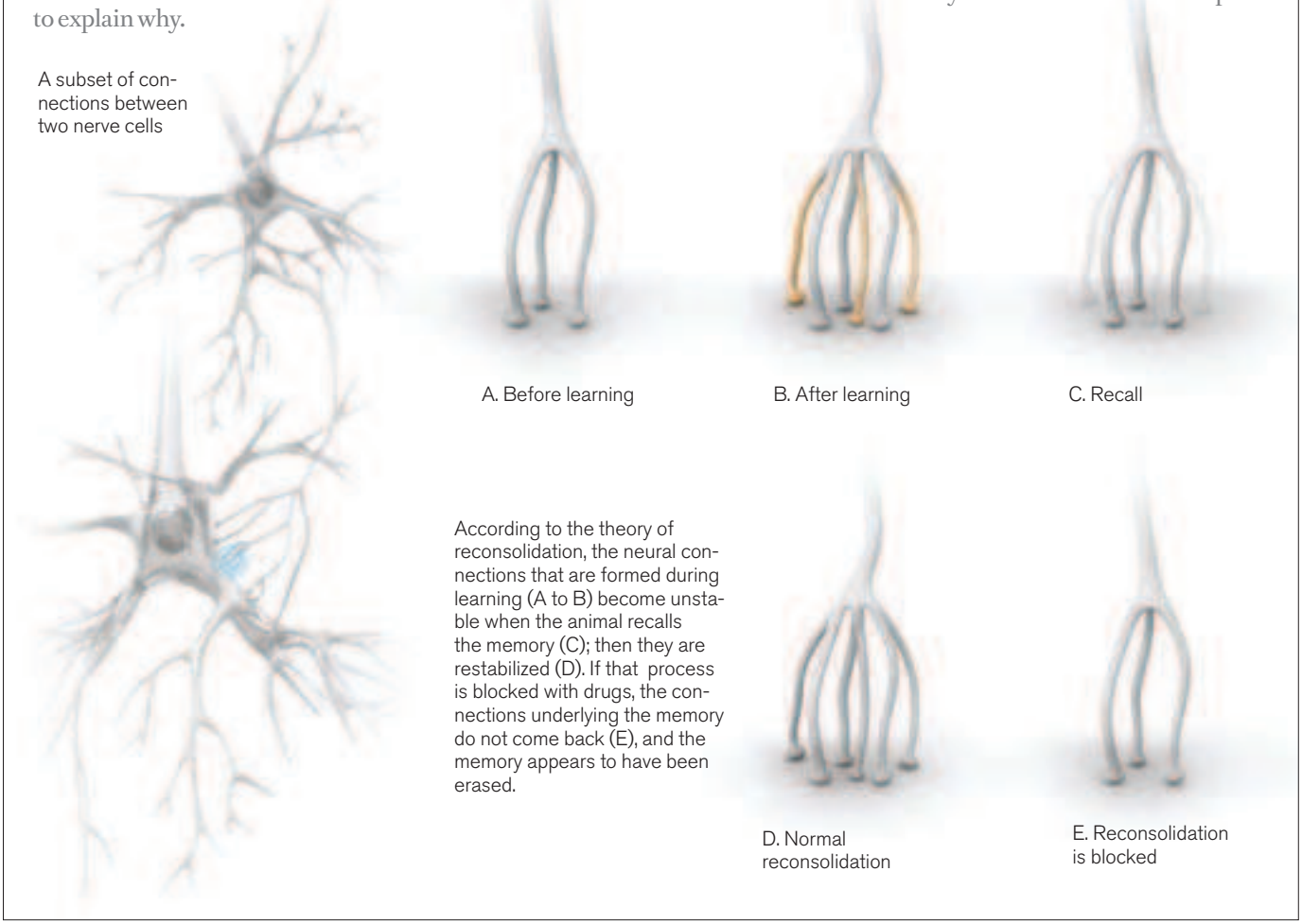
Brunet's office at the Douglas Institute in Montreal, its bright-orange walls adorned with paintings and greenery, emanates a cheeriness in stark contrast to the grim nature of his research. He decided to focus his career on PTSD while still a college student in the late 1980s at L'Ecole Polytechnique in Montreal, after a gunman entered an engineering class there and killed 14 women in a shooting rampage.

New treatments for PTSD are sorely needed. A recent study showed that about 15 percent of U.S. combat troops returning from the wars in Iraq and Afghanistan show signs of the disorder. And while some effective treatments exist, they consume a lot of time and resources, and they don't work for everyone.

Developing better therapies is easier, of course, if we know what causes the problem in the first place. One hypothesis holds that PTSD stems from a memory that is too strong, burned into the brain by hormones released in times of stress. These hormones, which surge as part of the body's fight-or-flight response, activate cells in a part of the brain responsible for the emotional component of memory. In an evolutionary context, enhancing the storage of frightening memories makes sense: the more vividly you remember scary situations, the more likely you may be to stay away from them in the future. But in PTSD, that process appears to have gone awry, producing pathologically powerful memories that are triggered by the smallest reminder. Researchers have had some success in preventing the formation of these supermemories by dampening the stress response soon after a trauma: Brunet and his colleague Roger Pitman, a psychiatrist at Harvard Medical School, have both shown that patients given epinephrine-blocking propranolol in the emergency room are less likely to develop PTSD. "The idea was that if you could decrease the release of stress hormones following a trauma, you could influence the saliency of that memory in the future," says Brunet.

THE THEORY OF RECONSOLIDATION

Memories are encoded at a cellular level as a complex set of connections between neurons. When an animal learns, for example, that a certain sound signals a food reward, new neural connections are made to solidify the memory. However, even stable memories can be vulnerable to erasure under certain circumstances. The theory of reconsolidation attempts to explain why.



This prevention strategy might work well in a military context, where everyone involved in a particular combat event could be given the drug, but it's not ideal for civilians. The time window for treatment is limited, and not everyone who experiences a trauma will rush to the ER. "Even treating people four to six hours after the trauma may be too late," says Pitman. If a treatment can't help them, it certainly can't help people who already have PTSD.

In 2004, Pitman—having learned of Nader's work—had another idea: to use propranolol to try to mimic animal research on reconsolidation, much of which has focused on fear memories. Researchers studying reconsolidation had previously suggested that blocking the reconsolidation of traumatic memories in people might help make these memories less troubling. Propranolol, it turns out, acts on the part of the brain that is central to the emotional component of memory—the same area targeted in Nader's rodent research. (Factual components of memory are stored in a different part of the brain.) By reactivating the patients' memories, Pitman proposed, "we could reopen the window of opportunity and get a second chance to treat PTSD."

A pilot study of the treatment found that propranolol did seem to soothe the anxiety provoked by patients' traumatic memories, long after the drug itself was gone from the body. In the study, patients wrote down their recollections of the trauma and then took a single dose of propranolol or a placebo. Those who received the drug were much calmer—as measured by heart rate and skin conductance—when reading a script of their stories a week later.

BRYAN CHRISTIE DESIGN

A larger study of about 60 people is now almost complete. Preliminary findings show a 40 to 50 percent improvement in self-reported symptoms among those taking the drug. At the end of the trial, nearly two-thirds of the patients in one of the groups taking propranolol no longer met the criteria for PTSD. The same was true for less than 10 percent of control patients.

Brunet pulls up a graph on his computer screen, its downward-slanting line reflecting the continued decline in the propranolol recipients' PTSD symptoms over the five weeks of the study. "We're seeing at least as good, if not better, results than people get with exposure treatment—and in much less time," he says. (In exposure treatment, one of the most common types of behavioral therapy for PTSD, patients repeatedly recall the details of their trauma with a therapist in a safe environment, eventually learning to dissociate the extreme fear from the details of the event.) And patients were still doing well four months after treatment, even though relapse is fairly common in PTSD therapy.

Though the results are preliminary (the treatment must still be tested in a proper double-blind study, in which neither patients nor physicians know who is getting the drug rather than the placebo), the work has attracted great interest. The U.S. Department of Defense has awarded Brunet, Pitman, and Nader a $7 million grant over four years to identify additional existing drugs that can target reconsolidation more effectively than propranolol. The study will focus on drugs that are already on the market, which means they are already deemed safe and can be tested in PTSD patients without additional animal testing. Pitman and his colleagues are currently testing opioids such as morphine in rodents. His group has also seen preliminary success in rodents with RU-486, the abortion pill; in addition to affecting progesterone, a hormone involved in pregnancy, the drug blocks the action of chemicals called glucocorticoids, which are found in the amygdala and play a role in the emotional aspect of memories.

Thumbing through a thick stack of grant applications on his desk, Brunet says he thinks that targeting reconsolidation will alleviate a range of problems beyond PTSD. "We might have discovered a new way of treating mental disorders," he says. "There are several disorders that have at their core a problem with emotional memories." Specifically, he says, "many types of addictions, while physiological, also include a psychological component."

While the role of memory may not be an obvious consideration in treating drug abuse, the sights, sounds, and smells that remind addicts of their habit are a strong trigger for relapse. Brain imaging studies demonstrate that if an addict is shown a trigger, such as a needle, the part of the brain associated with drug use immediately fires up. Psychiatrists have tried exposure therapy to rid addicts of these intrusive memories, with little success. However, studies show that blocking the reconsolidation of drug-linked memories works remarkably well in animals. In fact, says Barry Everitt, a neuroscientist at the University of Cambridge in England, "it's the only thing that works well."

www Karim Nader discusses memory manipulation in a video interview: **technologyreview.com/nader**

TRUE IDENTITY

Easing the pain of difficult memories sounds like a dream come true, perhaps even for people who don't suffer from anxiety disorders. But the idea also raises concerns. Such memories, after all, are an integral part of a person: frightening, sad, perhaps life-changing moments make up important chapters in the stories of our lives. We might not be the same if remembering these events felt no more emotional than recalling a trip to the grocery store.

But Brunet points out that he is trying to bring PTSD patients' memories into a normal emotional range, not blunt their power altogether. "Months after a breakup, when the pain is beginning to fade away, do you feel that you have lost something?" he asks. "Of course not. That's the fate of normal emotional memory." In PTSD, on the other hand, the memory is as painful and crippling as if the events had occurred yesterday, making it difficult to lead a normal life. He doesn't think that using propranolol to render these memories bearable would create any unique potential for abuse as a way to dull the regrets, fears, and embarrassments of everyday life; people already use alcohol and other drugs for such purposes.

The ethical worries may stem in part from a misunderstanding about the level of control that scientists have over memory. Researchers can manipulate memories only in very subtle ways. It's not possible to erase a web of interconnected memories, or to program people with substantial new memories. (Research into false memories and eyewitness testimony suggests that a memory can be subtly influenced: someone who has witnessed a car accident, for example, may estimate different speeds for the car depending on whether they are asked how fast they saw it "smash" or "bump" into a tree. But these changes are minor tweaks to existing memories.)

It's still too early to predict the ultimate impact that drugs and other treatments targeting reconsolidation will have on human memory. But for now, the power to block reconsolidation is giving scientists a new tool to probe the brain's storage system. Nader's next step is to use his research on reconsolidation to study how the brain files memories. If rats are taught two different associations—say, pairing a light with a shock and a sound with a shock—does blocking the reconsolidation of one memory affect the other? Experiments like this will begin to shed light on whether memories are stored according to when they were formed, the context in which they were formed, or other variables. Bit by bit, the answers to such questions should help unravel one of the most enticing mysteries of the mind. TR

EMILY SINGER IS *TECHNOLOGY REVIEW*'S SENIOR EDITOR FOR BIOMEDICINE.

Dissent Made Safer

HOW ANONYMITY TECHNOLOGY COULD SAVE FREE SPEECH ON THE INTERNET.

By DAVID TALBOT

"Sokwanele" means "enough is enough" in a certain Bantu dialect. It is also the name of a Zimbabwean pro-democracy website whose bloggers last year published accounts of atrocities by Robert Mugabe's regime and posted Election Day updates describing voter intimidation and apparent ballot stuffing. You can visit Sokwanele's "terror album" and see photographs: of a hospitalized 70-year-old woman who'd been beaten and thrown on her cooking fire (she later died, the site says); of firebombed homes; of people with deep wounds carved into their backs. You can find detailed, frequently updated maps describing regional violence and other incidents. You will be confronted with gruesome news, starkly captioned: "Joshua Bakacheza's Body Found."

Because this horrific content is so readily available, it is easy to overlook the courage it took to produce it. The anonymous photographers and polling-station bloggers who uploaded the Sokwanele material remain very much in danger. In a place like Zimbabwe, where saying the wrong thing can get you killed or thrown in prison on treason charges, you take precautions: you're careful about whom you talk to; you're discreet when you enter a clinic to take pictures. And when you get to the point of putting your information on the Internet, you need protection from the possibility that your computer's digital address will be traced back to you. Maybe, at that point, you use Tor.

Tor is an open-source Internet anonymity system—one of several systems that encrypt data or hide the accompanying Internet address, and route the data to its final destination through intermediate computers called proxies. This combination of routing and encryption can mask a computer's actual location and circumvent government filters; to prying eyes, the Internet traffic seems to be coming from the proxies. At a time when global Internet access and social-networking technologies are surging, such tools are increasingly important to bloggers and other Web users living under repressive regimes. Without them, people in these countries might be unable to speak or read freely online *(see "Beating Surveillance and Censorship," p. 64)*.

Unlike most anonymity and circumvention technologies, Tor uses multiple proxies and encryption steps, providing extra security that is especially prized in areas where the risks are greatest. Paradoxically, that means it's impossible to confirm whether it's being used by the Zimbabwean bloggers. "Anyone who really needs Tor to speak anonymously isn't going to tell you they use Tor to speak anonymously," says Ethan Zuckerman, cofounder of Global Voices, an online platform and advocacy organization for bloggers around the world. "You can't tell if it's happening, and anyone who is actively evading something isn't going to talk about it." That said, the Sokwanele journalists "are extremely sophisticated and use a variety of encryption techniques to protect their identity," he says.

Anonymity aside, Internet users in dozens of countries—whether or not they are activist bloggers—often need to evade censorship by governments that block individual sites and even pages containing keywords relating to forbidden subjects. In 2006, the OpenNet Initiative—a research project based at Harvard and the Universities of Toronto, Oxford, and Cambridge that examines Internet censorship and surveillance—discovered some form of filtering in 25 of 46 nations tested, including China, Saudi Arabia, Iran, and Vietnam.

In a new and still-evolving study, OpenNet found that more than 36 countries are filtering one or more kinds of speech to varying degrees: political content, religious sites, pornography, even (in some Islamic nations) gambling sites. "Definitely, there is a growing norm around Internet content filtering," says Ronald Deibert, a University of Toronto political scientist who cofounded OpenNet. "It is a practice growing in scope, scale, and sophistication worldwide."

Photograph by CHRIS CRISMAN

ANONYMIZER
Roger Dingledine is project leader of Tor, a system that obscures the true origin and destination of Internet communications.

Tor can solve both problems; the same proxies that provide anonymous cover for people posting content also become portals for banned websites. When it officially launched five years ago, the Tor network consisted of 30 proxies on two continents; now it has 1,500 on five continents, and hundreds of thousands of active users. And its developers are trying to expand its reach, both abroad and in the United States, because digital barriers and privacy threats affect even the free world. In the United States, for example, libraries and employers often block content, and people's Web habits can be—and are—recorded for marketing purposes by Internet service providers (ISPs) and by the sites themselves. "The Internet is being carved up and filtered and surveilled," says Deibert. "The environment is being degraded. So it's up to citizens to build technologies to [counter these trends]. And that is where I see tools like Tor coming into play. It preserves the Internet as a forum for free information."

NEUTRAL NODES

The product of a small nonprofit organization with eight paid developers and a few dozen volunteer security professionals around the world, Tor takes advantage of the fact that Internet traffic consists of two-part packets. The first part contains data—pieces of a Web page you are viewing, or of the photo file or e-mail you are sending. The other consists of the Internet protocol (IP) address of the sending and receiving computer (plus other data, such as the size of the file). Tor uses the latter portion—the addressing information—to build a circuit of encrypted connections through relays on the network (*see "Dodging Spies, Data Miners, and Censors," facing page*). The requisite relays (which collectively serve as proxies) are operated on a volunteer basis at universities such as Boston University and a few corporations, and by computer-security professionals and free-speech advocates around the world. (Many Tor users also use existing technologies, such as HTTPS—a protocol for encrypting and decrypting a user's page requests and the pages that are returned—to protect the content they are sending and receiving.)

Tor, like the Internet itself, emerged from military research—in this case at the U.S. Naval Research Laboratory in Washington, which built a prototype in the mid-1990s. The military interest was clear: without a way to make Internet traffic anonymous, an agent's cover could be compromised the minute he or she visited .mil domains using the Internet connection of, say, a hotel. Even if the data were encrypted, anyone watching traffic over the hotel network could quickly figure out that the guest might be associated with the U.S. military. And the problem is hardly limited to hotel networks; IP addresses can be linked to physical locations by a variety of means (ISPs correlate such data with phone numbers, data miners can piece together clues from Internet traffic, and someone outside your house can confirm that you are the source of specific kinds of Internet traffic by "sniffing" data traveling over Wi-Fi). As a Tor presentation puts it, chillingly, what might an insurgent group pay to get a list of Baghdad IP addresses that get e-mail from a .gov or .mil account?

The navy project never emerged from the lab, but it attracted the interest of Roger Dingledine, a cryptographer concerned about a different aspect of Internet privacy: the way ISPs and websites amass databases on people's browsing and search history. In 2000, at a conference where he was presenting his MIT master's thesis on anonymous distributed data storage, he met a Naval Research Lab mathematician, Paul Syverson. The two men saw that tools for protecting military agents and tools for protecting Web surfers' privacy could be one and the same, and together they revived the project with funding from the Defense Advanced Research Projects Agency (DARPA) and the navy.

The first public version of Tor, which came out in 2003, was available for anyone who cared to install it. But it worked only on open-source operating systems, and using it required at least some technical knowledge. The Electronic Frontier Foundation, the digital civil-liberties organization, funded development of a version for Windows, and soon a wider variety of users emerged. "Originally one of my big reasons for working on Tor was to provide tools for people in the West—Americans and Europeans—to let them keep their information safe from corporations and other large organizations that generally aren't very good at keeping it to themselves," says Dingledine, now 32, who is Tor's project leader. But now, he says, some police agencies use Tor to make sure that an investigation of an online scam won't be compromised by tipping the scammer off to regular site visits from a police department's computers. And some companies, he says, use it to help them prevent competitors from figuring out, say, who is scouring their online product sheets.

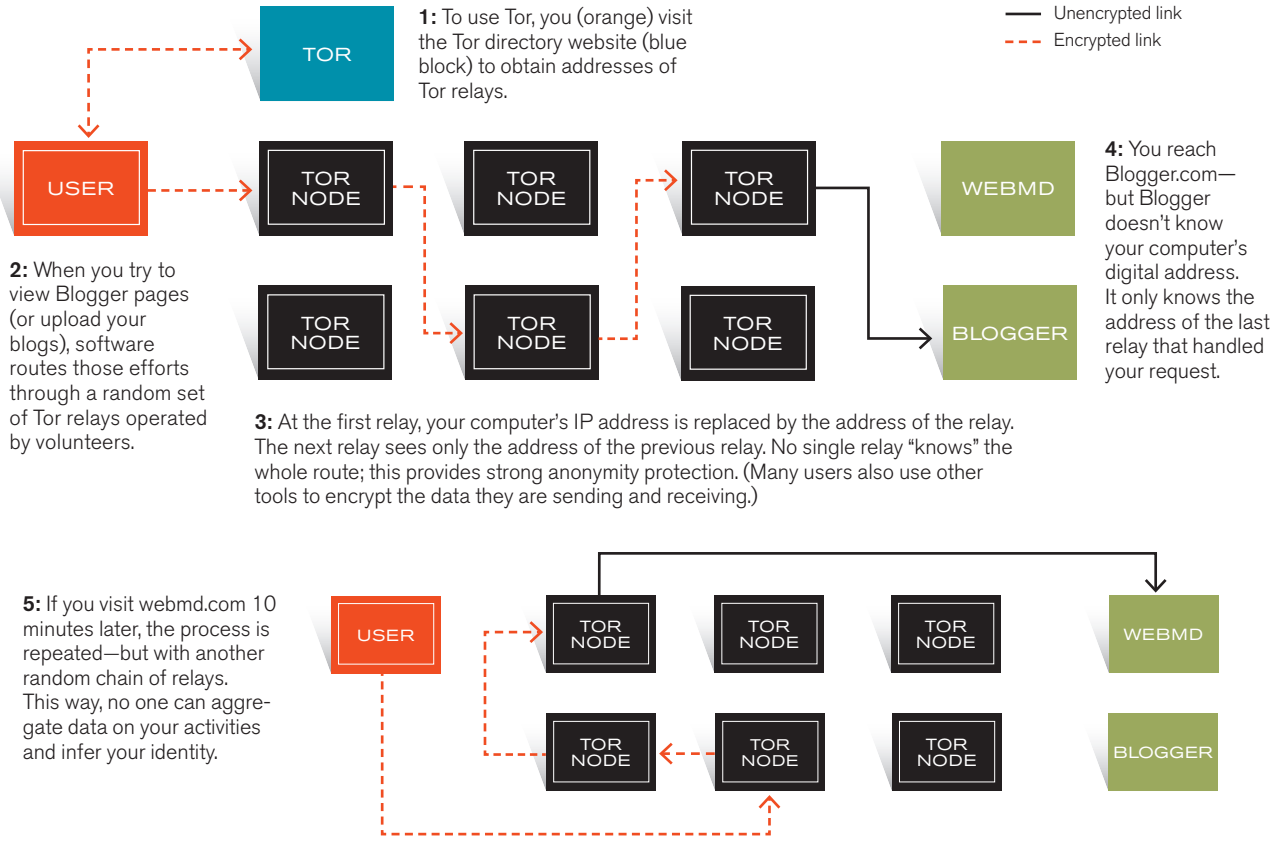
It quickly became clear that this diversity was crucial to the technology's success. "It's not just safety in numbers; there is safety in variety," Dingledine says. "Even if there were 100,000 FBI agents using Tor, you would know what it's for: 'You are using the FBI's anonymity system.' Even from the very beginning, part of the fun and the challenge was to take all of these different groups out there who care about what Tor provides, and put them all into the same network." To help promote wider use, its developers made Tor far easier to install. And in 2006, they developed a new feature, the Torbutton, which allows Tor users to easily turn Tor on and off while they browse with the Firefox Web browser (turning it off speeds up Internet access but removes the protections).

GLOBAL SPREAD

Syria is an all-purpose Internet repressor. It hunts down some bloggers; a Syrian named Tariq Biasi, for example, was recently sentenced to three years in prison for "dwindling the national feeling"; he allegedly posted a comment critical of the state's security service online. Beyond going after online critics, Syria also blocks many websites—including Facebook, YouTube, and Skype—from

DODGING SPIES, DATA MINERS, AND CENSORS

Let's say you want to visit www.blogger.com or www.webmd.com but don't want those sites (or your ISP) recording your computer's digital address as you do so. If you use Tor's Internet anonymity software, your computer's addressing data is encrypted at each of several relays. That way, a Web page can't track what computer is visiting, and someone watching your computer can't know what sites you are connecting to. The system can circumvent government filtering, too, because censoring countries generally block specific websites, not neutral and ever-changing Tor nodes.



all Web users in the nation. I spoke about Syrian censorship with another blogger, Anas Qtiesh; he sat in an Internet café in Damascus as I messaged him from my living room. Qtiesh isn't worried that he'll be tracked down, because he tends to blog about pan-Arab politics, not about criticisms of the regime. But he wants access to more of the Internet than the government permits, so the Firefox browser on his laptop sports the Torbutton. Click the button, and presto—the same Internet that everyone in America sees. To access blocked sites, his computer negotiates a series of proxies, eventually connecting to an IP address somewhere else in the world. This intermediary fetches the blocked material. "Tor brings back the Internet," he wrote.

Qtiesh has plenty of company: Tor was always of interest abroad, but word of mouth and the introduction of the easy-to-use Torbutton have helped accelerate its global spread. Zuckerman has been actively promoting Tor through his Global Voices network. So have other advocates of online free speech in Asia, China, and Africa. And these efforts have been working. Wendy Seltzer, who teaches Internet law at American University and founded Chilling Effects, a project to combat legal threats against Internet users, saw that firsthand when she traveled to Guangzhou, China, for a blogger conference last year. China is generally acknowledged as the most sophisticated Internet filterer in the world; it employs a variety of techniques, including blocking IP addresses, domain names

(the text name of a website, such as www.google.com), and even Web pages containing certain keywords (*Falun Gong*, for example). According to one report, Chinese security forces have arrested several hundred Internet users and bloggers in the past 10 years. Seltzer says that many bloggers she met in Guangzhou were using Tor. And when she went to an Internet café there, she reports, the computers were automatically configured to run the software.

In China, Tor is one weapon in a large arsenal. But in Mauritania, Tor appears to have single-handedly overwhelmed state censorship. Nasser Weddady is a Mauritanian-born son of a diplomat, now living in the Boston area. He is a civil-rights activist who seeks to call attention to the slavery still practiced in his native country, where black Muslims work in servitude for Arab and Moorish farms and households, far from the international spotlight. In 2005, in response to Internet filtering in Mauritania, he translated a guide to using Tor into Arabic and arranged for its distribution to owners of cybercafés. The effect was stunning: the government stopped filtering. Officials "didn't know we were using Tor," says Weddady. "I'm not sure they know what Tor is. But they noticed that our communications were not disrupted, so the filtering was useless."

Such successes can be short-lived, of course, and Weddady predicts that the regime will regroup and resume filtering. "The Middle East in general is a civil-rights desert; it has some of the most sophisticated filtering operations in the world," he says. "Plenty of people I personally know are using Tor in that region." Users know that to any snooper, the messages they post appear to originate from a Tor relay somewhere else in the world, so cybercafé owners can't rat them out even if they want to. "Tor doesn't say, 'Just trust us not to give out your information'—it says, 'We have a design where nobody is in a position to give up your information, because no one person has it,'" says Seltzer, who volunteers on Tor's board. "I do believe Tor is the best solution for people who are trying to get access to blocked matter, or are trying to speak anonymously."

BRIDGING TOR'S GAPS

Neither Tor nor any other tool is a perfect solution to Internet spying and censorship. As an open-source project, Tor publishes everything about its workings, including the addresses of its relays. That doesn't betray the actual source and destination of users' information, but it does mean that a government could obtain this list of addresses and block them. (So far, nobody has taken this step, though Iran, Saudi Arabia, and the United Arab Emirates did find a way to block Tor for a few months in 2008.) Second, using Tor can make Internet access painfully slow; online activities can take more than 10 times longer when using Tor, according to a study by Harvard's Berkman Center for Internet and Society. "It turns out the speed of light isn't so fast after all," Dingledine deadpans. And this problem is getting worse; in the past year, the number of users has increased faster than Tor's developers can add relays.

BEATING SURVEILLANCE AND CENSORSHIP

Here's how five leading tools rate in circumventing Internet censorship and protecting privacy. All use proxy computers in uncensored nations to help people in censored ones; Tor uses multiple proxies for extra protection.

Circumvention/anonymity tool	Source	Model	Strengths	Weaknesses
Tor www.torproject.org	Open-source nonprofit project, U.S. Navy research	Peer to peer, but with multiple hops through a network of proxies	Most secure for the most users	Slowest of the tested tools
Psiphon psiphon.ca	Citizen Lab at the University of Toronto	Peer to peer; users circumvent filters through one trusted proxy computer	No software installation required (users log in)	Slower than most tested tools
UltraReach www.ultrareach.com	UltraReach Internet	Centrally hosted, requiring trust in the company	Easy for users to install; fastest of tested tools	Requires funding to scale
Anonymizer www.anonymizer.com	Subsidiary of Abraxas	Centrally hosted, requiring trust in the company	Easy for users to install; can sustain growth	Retail version is insecure in countries that filter; free version available only in China and Iran
Dynaweb Freegate us.dongtaiwang.com/home_en.php	Dynamic Internet Technology	Centrally hosted, requiring trust in the company	Easy for users to install	Now available only in China; requires funding to scale

Sources: 2007 Circumvention Landscape Report: Methods, Uses, and Tools, Berkman Center for Internet and Society, March 2009; Hal Roberts

> "The Internet is being carved up and filtered and surveilled. The environment is being degraded. So it's up to citizens to build technologies to [counter these trends]."

But the biggest limitation is simply that all these tools still reach only a narrow slice of the world's Internet users. Yes, if you're a business traveler in China and have technical savvy and bandwidth—or you hire someone to set you up—you can circumvent government filters. (It's generally understood that state security forces will rarely move to shut down circumvention tools unless they're publicly embarrassed by being outsmarted online.) But a recently released Berkman report by Zuckerman, faculty codirector John Palfrey, and researcher Hal Roberts has concluded—on the basis of data supplied in 2007 by makers of circumvention software—that only a few million people use the major circumvention tools worldwide. It's true that usage has grown since then—and this estimate doesn't count everybody who has figured out a way to use proxies. Still, China alone has 300 million Internet users, and the researchers believe that most of them aren't equipped to fight censorship. Meanwhile, the list of nations that censor is only growing. Two years ago, Turkey piled on, with particular zeal for stamping out criticism of the nation's founding father, Kemal Atatürk.

Tor is preparing for the fight against relay blocking by creating a system of "bridge nodes"—a constantly changing list of IP addresses through which people can reach the main network of relays. A user can simply send an e-mail asking for a bridge address. Of course, an Iranian censor could also request and block such addresses, but the idea is to defeat such efforts by generating ever more bridges, donated by a wide range of Internet users. And Jonathan Zittrain, a Berkman cofounder and Harvard Law School professor, envisions going even further. "The next big moment that the Tor people haven't implemented—something in the background, something that would be huge—would be if your use of Tor, by default, makes you a Tor node yourself," he says. "At that point, it totally scales. The more people use it, the more people can use it."

As part of a three-year effort to improve the software and expand its use, Tor's staff and volunteers will step up appeals for Tor users to let their computers serve as bridges to individual users elsewhere. But taking the next step—becoming a relay, or node, potentially available to any Tor traffic—would massively increase the traffic flowing through a user's computer. If users became nodes by default, it could defeat the purpose of using Tor to remain low key: once a user wandered into a cybercafé to blog anonymously, that terminal would soon stand out as a hub of Internet traffic. What's more, such a system "sets off an arms race with all the network providers and network administrators," says Andrew Lewman, Tor's executive director. "It increases traffic, and we become something they might block, because that's their job." Tor would ultimately like to find safe ways to enlist distributed help, but for now, developers are pursuing intermediate goals, such as limiting bulk data transfers and improving the flow among existing Tor relays.

One criticism leveled against Tor is that it can be used not only for good purposes but for bad—protecting distributors of child pornography, for example. Dingledine's response is that Tor's protections help law enforcement catch criminals, too, while criminals may find it more effective to use neighbors' or public Wi-Fi links, or hacked computers, to mask their identities.

Another concern is that circumvention tools—especially those that only use a single proxy, which holds information about who is talking to whom—can create privacy and security worries of their own. Earlier this year, Hal Roberts discovered that certain tools used widely in China—DynaWeb Freegate, GPass, and FirePhoenix—appeared to be offering to sell users' browsing histories. While there's no evidence that any individual's privacy was compromised, the point was made: in many cases, using anonymity or circumvention systems still means trusting an organization with your information—and trusting that its privacy policies can and will be honored. (With Tor, it's a bit different; since no single relay ever holds the information about the complete route, you must trust the integrity of algorithms that obscure connections between origins and destinations.) "I don't doubt the dedication of the people hosting these tools, but what I'm concerned about is whether they will protect your data," Roberts says. "The biggest takeaway is: they have that data."

Dingledine thinks events will push people to seek the protections that Tor and other tools provide. In 2006, for example, AOL gave away millions of users' search terms for research purposes. Although the searchers were identified only by random numbers, bloggers and reporters were quickly able to identify individual users from clues based on the search terms. (Since Tor uses a different router pathway for each user each time, it's impossible to amass such aggregate data about even an anonymously identified Tor user.) Dingledine reasons that each time a national censor blocks news sites and YouTube, or an ISP or website loses or sells or gives away user data, people will seek solutions. "The approach we've taken so far is to let the bad guys teach people about it," he says. "Let the AOLs and the China firewalls screw up. Let everybody read about why they want privacy on the Internet." More and more people might just decide that enough is enough. TR

WWW

See how Tor works, and hear Roger Dingledine explain its development: **technologyreview.com/tor**

DAVID TALBOT IS *TECHNOLOGY REVIEW*'S CHIEF CORRESPONDENT.

ESSAY

First Life and Next Life

SYNTHETIC BIOLOGY IS A NEW FIELD, BUT IT'S TARGETING AN OLD QUESTION: HOW DID LIFE BEGIN?

By DAVID DEAMER

The driver turned off the engine of his rumbling Russian-army troop carrier at the edge of a deep canyon carved by a stream of glacial meltwater. Our little research group—which included Stanford graduate students Jamie and Meaghan, postdocs Jan and Jake from the Carnegie Institution of Washington, and our guide, Vladimir—clambered down from the truck for a welcome stretch after a jarring five-hour drive from Petropavlovsk. Then we shouldered our packs and began to climb, crunching over packed snow and ice between house-size boulders. When we stopped for breath and looked back downhill, we could see the ash and lava flows from past eruptions eroded into hills and valleys, with scattered patches of low shrubs in sheltered areas far below. The jagged volcanic landscape of Kamchatka defined the horizon. Above us loomed our goal: the blasted peak of Mount Mutnowski, a volcano that had erupted just a few years before.

Two hours later and 2,000 feet higher, we peered over the edge of the crater. It was hard to grasp the chaos beneath us. There was nothing alive in this landscape of black and gray rock except our team of six. A small glacier on the other side was melting into the crater, and distant roaring sounds emanated from deep inside as steam rose into the blue sky. Earth, air, fire, and water, I thought—the ancient elements, brought together here in far eastern Russia, stirred by heat energy left over from the beginning of our planet's history. Except for the glacier, this place seemed like a remnant from that time—a model of what Earth was like four billion years ago, before life began. We made our way down into the crater, at times wearing gas masks to protect our lungs against caustic gases.

My fieldwork in Kamchatka was supported by a NASA grant, and our main goal was to better understand geochemical conditions related to the origin of life on Earth and perhaps on Mars. Earlier publications in Russian-language journals had reported that organic compounds, including amino acids, were present in the boiling springs and vapors of volcanoes in Kamchatka. Everyone agrees that the origin of life required a source of organic compounds, but no one really knows what the primary source might have been. One possibility is that most of the compounds were produced by geochemical synthesis in volcanic regions early in Earth's history, and it would be a real breakthrough if we could detect similar reactions in volcanoes today.

The second goal was basically to hedge my bet. What if we got all the way to Kamchatka and found no organic compounds? That would be embarrassing. For this reason I brought along a mixture of compounds similar to those we thought might have been available four billion years ago to kick-start life: four amino acids, a fatty acid, phosphate, glycerol, and the four bases of nucleic acid. We knew that under laboratory conditions, these components can react to produce more-complex compounds related to the molecular structures and functions characteristic of life. I proposed to add these to a volcanic pool to see what would happen. Most of my colleagues believe that this kind of experiment is a bit silly because the conditions are so uncontrolled, but I think of it as a reality check. We can get interesting reactions to work in a laboratory, but what if we are overlooking something that becomes apparent only when we try to simulate those reactions in a natural environment?

SYMBIOSIS AND SYNTHETIC BIOLOGY

When I first began to hear the term *astrobiology* a few years ago, it sounded strangely discordant. And then another new discipline appeared that was even more of a stretch: *synthetic biology*. But this is how science progresses—by a kind of symbiosis between seemingly unrelated disciplines, in which traditional biology and chemistry become biochemistry, and biology and physics become biophysics. I began my career

Illustration by CHRIS BUZELLI


BUZELLI

doing traditional biophysical studies on membranes, but now some of my research is funded by NASA's astrobiology program, and many of our experiments could be described as synthetic biology: the application of engineering techniques to design or redesign biological functions and systems.

The field of synthetic biology is hot just now, because its methods are potentially very powerful. Synthetic biologists know enough about living systems to alter genetic programs in useful ways, the way expert computer programmers alter software. But what does such high-tech science have to do with volcanoes and the origin of life? Louis Pasteur once commented that chance favors the prepared mind; very often, even the most basic research produces an undreamed-of application. For example, one of the most powerful tools of molecular biology is the polymerase chain reaction (PCR), which is used to amplify DNA—that is, to make multiple copies of a given sequence. In PCR, cycles of heating and cooling combine with DNA synthesis by a polymerase, an enzyme that catalyzes the building of large molecules (polymers) from small molecules (monomers). Kary Mullis came up with the idea in 1983, first using a polymerase from ordinary *E. coli* bacteria, but a polymerase was needed that could survive near-boiling temperatures. In 1965—in completely unrelated research—Thomas Brock discovered a primitive bacterium, which he named *Thermus aquaticus*, living in the volcanic hot springs of Yellowstone National Park. This organism is the original source of the heat-resistant *Taq* polymerase now used in all commercial PCR devices.

If we follow Pasteur's advice, we can increase the chances for more such serendipitous discoveries. In particular, we can prepare our minds by broadening the scope of synthetic biology to encompass studies of the origin of life. I will begin by describing nature's version of synthetic biology; then I will show how our growing understanding of life's molecular mechanisms suggests a way to reproduce the origin of life in the laboratory.

FIRST LIFE: SYNTHETIC BIOLOGY IN THE WILD

To take on the question of life's origin, we need to have some idea of what Earth was like four billion years ago. There is good evidence that oceans were already present, predating life by several hundred million years. The oceans were salty, probably somewhat acidic, with volcanic land masses rising above sea level. Precipitation onto those islands produced freshwater ponds, so a marine environment is not the only one in which life could have begun. The atmosphere was a mixture of carbon dioxide and nitrogen, with little or no oxygen, and the average global temperature was 60 to 70 °C, much higher than today's 15 °C. Thus the first forms of life probably resembled the thermophilic bacteria that inhabit hot springs today.

How could life begin in such an unpromising environment?

A LABORATORY, OF SORTS The author sampling boiling fumaroles in the crater of Mt. Mutnowski, in Kamchatka, Russia.

Charles Darwin occasionally wondered about that, though he was too conservative to speculate in public about the origin of life. In a private letter to his friend Joseph Hooker, he wrote: "But if (and Oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc., present, that a protein compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed." And his great book *On the Origin of Species* touches on the question in a single sentence: "Looking to the first dawn of life, when all organic beings, as we may believe, presented the simplest structure, how, it has been asked, could the first steps in the advancement or differentiation of parts have arisen?"

Less eloquently, what would be required for the evolution of life to begin? First of all, evolution works on populations, not single organisms, so we need to find a way to generate large numbers of molecular systems in the prebiotic environment. Furthermore, there must be great variation in their properties. The requirement of variation within a population means that the first life forms capable of evolution could not be random mixtures of replicating molecules unable to assemble into discrete entities; instead, they would be systems of interacting molecules encapsulated in something like a cell.

The systems would have to exhibit the two primary functions of life: growth and reproduction. Cells grow by taking in nutrients—simple molecules from the environment. They use energy to link those molecules into the polymers that we call proteins and nucleic acids. Reproduction requires a mechanism by which genetic information can be stored and then replicated, so that the information, in the form of genes, can be passed on. But the transfer of information is necessarily imperfect. A certain number of errors—mutations—must occur to produce variations in the population such as those that enabled primitive life to explore different niches and begin evolving toward the magnificent biosphere of today's Earth.

COURTESY OF DAVID DEAMER

We're talking about forms of life much simpler than even the most primitive bacteria that exist now. Still, how could cells of any kind spontaneously appear out of random mixtures of simple organic molecules? The prospect is so mind-boggling that a few scientists state flatly that we will never understand how it came about. I'm more optimistic. But attempting to discover how life began is hard work, with no certainty that we will ever find answers. We need to formulate and test hypotheses, and be willing to venture into vast unexplored territory. I will briefly describe some of the milestones on this journey. As we acknowledge them, we can begin to assemble a logical cage that constrains speculation and guides us toward answers.

FIRST MILESTONE: A SOURCE OF ORGANIC MONOMERS

The four basic varieties of biomolecules are amino acids and proteins, carbohydrates, nucleic acids, and lipids. There is little doubt that similar—even identical—organic compounds were present in the prebiotic environment. That was the conclusion of Stanley Miller's famous experiment in the early 1950s in which he exposed mixtures of ordinary gases to electrical discharges and observed the formation of amino acids. Since that time, virtually all the primary carbon compounds of life have been synthesized in prebiotic simulations.

The results of simulation studies were strongly supported when a remarkable meteorite fell to Earth near Murchison, Australia, in September 1969. It was clear that the meteorite contained organic material, because a strange smell emerged from the hot surfaces. Forty years later, when I grind Murchison samples in the lab, the same odor wafts up from the mortar—simultaneously dusty, oily, and sour. This is an ancient odor, older than Earth itself, preserved for five billion years in a comet or asteroid from which the original meteorite was derived.

There are thousands of organic compounds present in the Murchison meteorite and other carbonaceous meteorites that have been analyzed—confirming Miller's experiment by showing that biologically relevant organic compounds are in fact produced by nonbiological processes. This makes it plausible that organic compounds were present on prebiotic Earth, either synthesized by geochemical processes or delivered as meteoritic and cometary infall more than four billion years ago.

SECOND MILESTONE: SELF-ASSEMBLY OF COMPARTMENTS AND PROTOCELLS

The unit of all life today is the cell. My research background is in membrane biophysics, and I began my career by studying the lipid membranes that are the essential boundaries defining living cells. Twenty years ago, when I obtained a golf-ball-size stone from the Murchison meteorite, I wanted to see whether anything resembling lipids was present in the mix of meteoritic organics, perhaps shedding light on how life became cellular.

In earlier research I had often used a mixture of chloroform and methanol to extract lipids from a variety of biological materials, such as red blood cells, chloroplasts, mitochondria, and even egg yolks—the last being a rich source of a phospholipid called lecithin. And in 1975 I had spent a sabbatical leave in the lab of Alec Bangham, who discovered in the 1960s, working at a research institute near Cambridge, England, that lecithin could spontaneously self-assemble into membranous sacs, or vesicles, that have come to be called liposomes. I now employed the chloroform-methanol mixture to isolate compounds from samples of the Murchison stone, then used a chromatographic procedure to purify those that might be capable of self-assembly into membranes. The left panel in the figure on page 71 shows what happened when a few micrograms of the extract were dried on a microscope slide and exposed to water to simulate the cycles of wetting and drying that would have been frequent on the early Earth. The results were very exciting. Not only were lipidlike molecules present in the mix, but they readily self-assembled into cell-size vesicles.

When we analyzed the mixture of meteoritic organics, we found that some of the compounds were short-chain fatty acids, soaplike molecules that feature a tail of 9 to 13 carbon atoms. This meant that we no longer needed material from precious meteorites to carry out experiments; we could investigate the properties of the pure compounds purchased from chemical-supply companies. We began with decanoic acid, a 10-carbon fatty acid, and found that it readily produced vesicles similar to those produced by the meteorite extracts. The next question was whether such compartments could encapsulate larger molecules to produce protocells, which are defined as encapsulated systems of molecules—like RNA—that have the potential to act as catalysts and carriers of genetic information. This turns out to be so easy that it could be done for a high-school science fair. If the microscopic vesicles are mixed with large molecules like proteins or nucleic acids, then put through a dry-wet cycle, about half of the large molecules end up inside the vesicles. The glowing lipid vesicles shown in the right-hand panel of the micrograph are composed of decanoic acid surrounding DNA molecules.

The bottom line is that protocells are very easy to produce by simple self-assembly processes. It follows that such structures would also be expected to occur in a prebiotic setting.

THIRD MILESTONE: POLYMER SYNTHESIS

All life today uses enzymes to catalyze the synthesis of polymers. And nearly all polymeric molecules of life, including proteins and nucleic acids, are synthesized from monomers

that are chemically activated—that is, they gain the energy to undergo polymerization—through complex metabolic processes that extract the equivalent of a water molecule from each one. Ribosomes link activated amino acids through peptide bonds to produce proteins, and enzymes called polymerases catalyze the formation of ester bonds between activated nucleotides to produce nucleic acids.

Nothing nearly this complicated could have happened before life began, but a variety of simpler reactions can also produce interesting polymers. For instance, James Ferris, at Rensselaer Polytechnic Institute in New York, showed that a clay mineral called montmorillonite promotes the synthesis of polymeric RNA from activated nucleotides. The mineral surfaces adsorb and organize the nucleotides, which then zip up into polymers. Furthermore, once RNA molecules are formed, they can undergo a kind of limited replication process that does not require enzymes. Leslie Orgel and his associates at the Salk Institute demonstrated in the 1980s that chemically activated nucleotide monomers line up on synthetic RNA templates by Watson-Crick base pairing, as they do in the double helix of DNA, and then polymerize into a second strand of RNA.

The seminal observations of Orgel, Ferris, and others clearly suggested that something like RNA might have been the first polymer to be associated with life processes. Additional evidence was provided when Thomas Cech at the University of Colorado and Sidney Altman at Yale found that certain types of RNA had catalytic properties, a discovery for which they shared a Nobel Prize. Such RNA molecules, now referred to as ribozymes, can make and break specific chemical bonds within their own structure rather than depending on protein enzymes. The discovery of catalytic RNA led Nobel-winning chemist Walter Gilbert at Harvard to propose an "RNA World," positing that life did not begin with the complex systems of DNA, RNA, and proteins that characterize all life today. Instead, RNA molecules could have served as catalysts as well as storing and transmitting genetic information. The RNA World concept dominates current thinking about the origin of life. Research groups led by Gerald Joyce at the Scripps Research Institute, David Bartel at the Whitehead Institute, and Peter Unrau at Simon Fraser University are attempting to incorporate RNA into a self-replicating system of molecules. Significantly, they often employ a technique in which evolutionary principles are used to select specific catalytic activities from mixtures containing trillions of different RNA molecules.

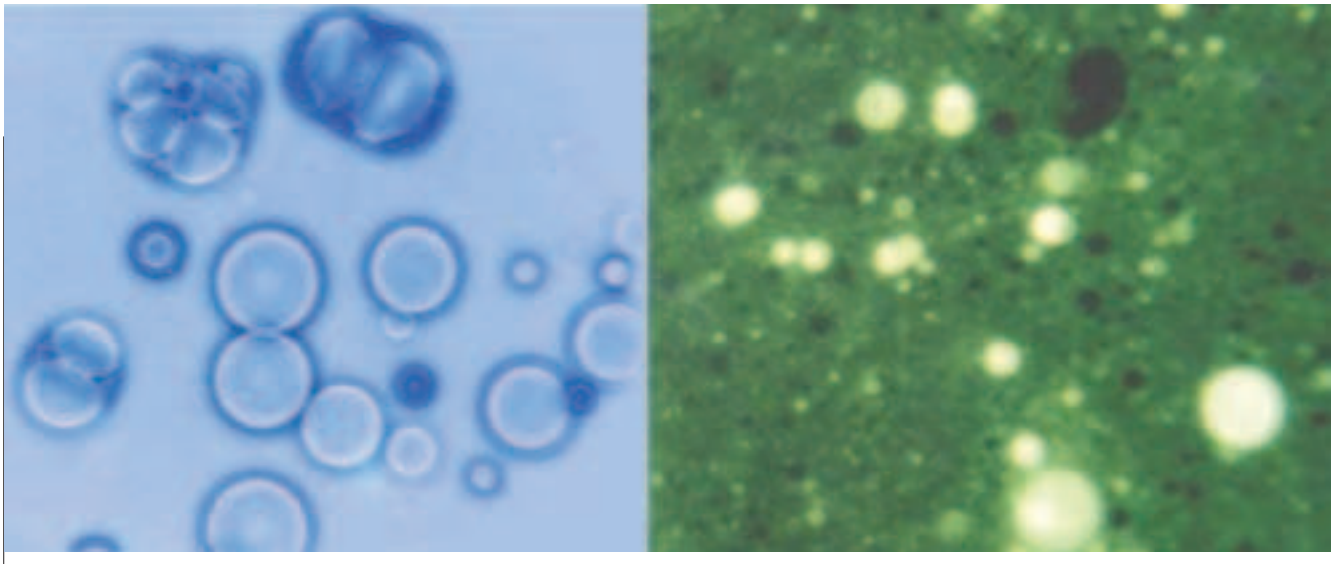
That brings us to the next milestone.

FOURTH MILESTONE: EVOLUTION OF CATALYSTS

Can genetic information somehow emerge in random mixtures, essentially by chance? If the answer is no, then we're in trouble, because those of us who work on the origin of life claim that this is exactly what happened four billion years ago, when the first forms of life emerged from a sterile mixture of minerals, atmospheric gases, and dilute solutions of organic compounds. To address that question, I will revisit a classic experiment that David Bartel and Jack Szostak published in 1993, while Bartel was a graduate student in Szostak's lab. Their experiment is moderately complicated, but the result is so important that it is worth explaining here. The goal was to see if a completely random system of molecules could undergo evolutionary selection in such a way that molecules with catalytic properties could evolve. The first step was to synthesize trillions of different RNA molecules consisting of approximately 300 nucleotides, arranged in random sequences. Bartel and Szostak reasoned that buried in those trillions were a few ribozymes that happened to catalyze a ligation reaction, in which one strand of RNA is linked to a second strand. They developed a procedure that captured those rare molecules even if they only weakly catalyzed the reaction. Then they used enzymes to amplify them. The amplified sequences were put through another round of selection and amplification, and the process was repeated for 10 cycles.

The results were stunning. Increased catalytic activity began to appear after four cycles, and after 10 rounds the rate of catalysis was seven million times the uncatalyzed rate! It was even possible to watch the RNA evolve. Nucleic acids can be labeled with radioactive phosphate, then separated and visualized through a technique called gel electrophoresis. A mixture of RNA molecules is placed at the top of a gel and a voltage of several hundred volts is applied, which causes the molecules to migrate downward through the gel. Larger molecules don't move very far, so they appear as bands near the top of the gel; smaller, faster-moving molecules form bands near the middle and bottom. At the start of the experiment, nothing could be seen in the gels, because the RNA molecules were all different. But after three cycles, distinct bands appeared, meaning that certain catalytic species were already being selected. With further cycling, other species appeared for a few cycles and then went extinct. After 10 cycles, two distinct RNA species survived, representing those RNA molecules that were most efficient in catalyzing the ligation reaction.

These results demonstrate a fundamental principle of evolution at the molecular level. At the start of the experiment, every molecule of RNA was different from all the rest, but then a selective hurdle was imposed in the form of a ligation reaction that allowed only certain molecules to survive and reproduce. The result was that specific catalytic molecules emerged by a process closely reflecting Darwinian natural selection. The conclusion: genetic information can in fact appear in random mixtures, as long as the mixtures begin with large numbers of



OLDER THAN EARTH! When the author extracted certain molecules from a five-billion-year-old meteorite and let them get wet, they self-assembled into cell-like vesicles (left). He also found that decanoic acid, a fatty acid present in the meteorite, readily forms similar vesicles—ones capable of encapsulating DNA (glowing, right).

polymers defined by a variety of nucleotide sequences from which specific sequences having a catalytic property can be selected and amplified. It seems reasonable to propose that similar selective processes could have occurred on the prebiotic Earth when the first forms of life self-assembled in a mixture of organic compounds and then began to evolve.

FIFTH MILESTONE: COMBINATORIAL CHEMISTRY & GARBAGE BAGS

Most chemists learn to do their experiments in series, one per day. But experiments can also be done in parallel with a technique called combinatorial chemistry. This approach is particularly useful in the pharmaceutical industry, in which it is often necessary to experiment with large numbers of compounds in order to optimize a reaction or test a new drug. A robotic device loads hundreds or even thousands of small reaction chambers with the desired mixtures, each chamber containing a droplet that is slightly different from the rest. After the reaction is completed, the chambers are individually tested for activity.

In my lab, we perform a version of combinatorial chemistry when we prepare liposomes by adding water to a few milligrams of dry lipid in a flask. A milky suspension is produced that contains, not thousands, but trillions of individual microscopic vesicles in the size range of small bacteria—half a micrometer in diameter. If the vesicles are prepared in a solution containing small peptides and short nucleic acids such as RNA, each of the vesicles will contain a different set of components, so each represents a microscopic experiment. Now let's think about the early Earth. Instead of milligrams of lipid in a flask, it would have had billions of tons of organic material assembling into enormous numbers of microscopic structures, and half a billion years to do the experiment.

The origin of life can be understood metaphorically as combinatorial chemistry on a global scale. A few of the microscopic experiments must have been successful, resulting in primitive cells capable of capturing energy and nutrients in order to grow by means of polymerization reactions. Evolution began when the cells filled a limited niche and competed for resources. At that point, natural selection took over, placing a premium on how efficiently a given cell could capture nutrients in order to grow. I imagine that once robust cellular life got under way, it expanded exponentially. Earth, seen from space, may even have blushed red or turned green for a while when photosynthetic bacteria filled the oceans.

Will we ever discover the combination of ingredients that gave rise to life? Again, I am optimistic. We need to apply what we know about the chemistry and physics of living systems to narrow down the possibilities, then be brave enough to actually do some experiments. But what experiments should we try? This is where theory can guide us. Freeman Dyson, one of the great theoretical physicists of our time, has also taken an interest in the origin of life. In his book *Origins of Life,* Dyson succinctly summarizes what I have told you:

> Life began with little bags, the precursors of cells, enclosing small volumes of dirty water containing miscellaneous garbage. A random collection of molecules in a bag may occasionally contain catalysts that cause synthesis of other molecules that act as catalysts to synthesize other molecules, and so on. Very rarely a collection of molecules may arise that contains enough catalysts to reproduce the whole population as time goes on. The reproduction does not need to be precise. It is enough if the catalysts are maintained in a rough statistical fashion. The population of molecules in the bag is reproducing

DAVID DEAMER

itself without any exact replication. While this is happening, the bag may be growing by accretion of fresh garbage from the outside, and the bag may occasionally be broken into two bags when it is thrown around by turbulent motions. The critical question is then, what is the probability that a daughter bag produced from the splitting of a bag with a self-reproducing population of molecules will itself contain a self-reproducing population? When this probability is greater than one half, a parent produces on the average more than one functional daughter, a divergent chain reaction can occur, the bags containing self-reproducing populations will multiply, and life of a sort has begun.

The life that begins in this way is the garbage-bag world. It is a world of little protocells that only metabolize and reproduce themselves statistically. The molecules that they contain do not replicate themselves exactly. Statistical reproduction is a good enough basis for natural selection. As soon as the garbage-bag world begins with crudely reproducing protocells, natural selection will operate to improve the quality of the catalysts and the accuracy of the reproduction. It would not be surprising if a million years of selection would produce protocells with many of the chemical refinements that we see in modern cells.

NEXT LIFE: SYNTHETIC CELLS

Theoretical concepts like the RNA World and Dyson's garbage-bag world have inspired experimental approaches in which systems of molecules enclosed by membranes are sufficiently complex to have some of the properties of life. The ultimate goal is to assemble a cellular system that can use energy to grow through a process of catalyzed polymerization, replication of genetic information, and evolution. Several laboratories have initiated such studies, and there is reason to believe that the goal of artificial life may be achieved in the next decade. I will now recount a brief history of research on fabricating artificial cells.

Perhaps the first thing to understand is that assembling a system of molecules capable of reproducing is old news. More than 50 years ago, Heinz Fraenkel-Conrat and Robley Williams at Berkeley discovered that the tobacco mosaic virus could be separated into its coat protein and RNA. If the two components were mixed together, they reassembled into the infectious agent. More recently, in a remarkable display of modern molecular-biology methods, Jeronimo Cello, Aniko Paul, and Eckard Wimmer at the State University of New York at Stony Brook fabricated a functional polio-virus genome by stitching together hundreds of smaller fragments that were synthesized using chemical techniques. And two years ago Hamilton Smith and his colleagues at the J. Craig Venter Institute in Rockville, MD, managed to synthesize a complete genome of a small bacterial species called *Mycoplasma genitalium*. The uproar this caused is an indication of what will face the first claims that a living cell has been reassembled from its parts.

The synthesis of viral and bacterial genomes suggests that even more-challenging fabrications may be possible. We have known for years that spontaneous self-assembly processes can produce surprisingly complex systems of functional molecules. Efraim Racker, working at Cornell University, pioneered the effort to dissect and reconstitute mitochondrial membranes in the 1970s. Mitochondria are subcellular organelles that are present in most cells, and embedded in their membranes are enzymes that remove electrons from metabolic products derived from nutrients such as glucose. The process is called electron transport, because the electrons then pass through a chain of enzymes in the mitochondrial membrane and are delivered to oxygen. The electron transport is tightly coupled to a second transport process, in which positively charged protons derived from water are pumped outward, producing an electrical potential of approximately 0.2 volts across the membrane. This voltage provides the energy source for the synthesis of adenosine triphosphate (ATP), which transports chemical energy within cells and therefore drives most life processes. The universal mechanism by which ATP is synthesized, now referred to as chemiosmosis, was proposed in 1961 by Peter Mitchell, a remarkable British scientist who later carried out research in his home in Bodmin, Cornwall.

Racker and his students dissolved mitochondrial membranes with a detergent called deoxycholic acid. One of his first discoveries was that the membranes contained an enzyme that coupled ATP synthesis to electron transport. He referred to this as a coupling factor, but it is now called an ATP synthase. Racker also found that the detergent could be removed by dialysis—simply by placing the clear solution in a bag composed of a material resembling cellophane and letting it sit overnight in a dilute salt solution. The small detergent molecules leaked out of the bag, but larger molecules could not get through the porous material. The next day the solution was turbid, because membranous vesicles containing the original protein components had reassembled. The vesicles were fully capable of electron transport reactions and ATP synthesis. It was the first reconstitution of a very complex biological function.

At about the same time, Walther Stoeckenius at the University of California, San Francisco, became curious about the pigmented membranes of a bacterial species called *Halobacterium halobium*, which lives in extremely salty water. Stoeckenius and Dieter Oesterhelt were able to isolate the purple pigment—bacteriorhodopsin—and found that its function

was to absorb light energy and use the energy to transport protons across the bacterial membrane. The energy of the proton gradient was then used to synthesize ATP. Racker and Stoeckenius, both members of the National Academy of Sciences, then initiated a rare collaboration between two senior scientists. They used Racker's dialysis method to reconstitute a system of membranous vesicles containing only the proton pump of purple membranes and the ATP synthase of mitochondria. In 1974, they reported that the hybrid vesicles could use light as an energy source to synthesize ATP. Their paper added to the weight of evidence that finally confirmed chemiosmotic synthesis of ATP, for which Peter Mitchell was awarded the Nobel Prize in 1978.

The point of this brief history is that a surprisingly complex biological function can be reconstituted through self-assembly of dispersed components. Why not try to reconstitute a whole cell? If this turns out to be possible, perhaps it will help us untangle what we mean by "life" and even elucidate the major steps that led to the origin of cellular life.

Pier Luigi Luisi and his research associates in Zurich made the first attempt by encapsulating ribosomes in lipid vesicles in 1999, together with a synthetic form of RNA that told the ribosomes to incorporate the amino acid phenylalanine into a protein. A few short peptides were produced, but lipid bilayers are impermeable to amino acids, so synthesis was limited to those phenylalanines that happened to be inside the vesicles. Vincent Noireaux and Albert Libchaber at the Rockefeller University had a clever solution for the permeability problem: why not add a channel to the lipid bilayer of the vesicles? They reported in 2004 that they had succeeded in encapsulating a complete translation system isolated from *E. coli*, along with messenger RNA that directs ribosomal synthesis of green fluorescent protein (GFP) and of hemolysin, a protein that serves as a channel allowing externally added amino acids and ATP to enter the vesicles. The system worked for as long as four days, and at the end of the incubation period the vesicles glowed green from the accumulated GFP. Tetsuya Yomo and his research group at Osaka University have gone a step further with a similar encapsulated translation system in which the GFP gene is present in a strand of DNA. They refer to their system as a genetic cascade, because the GFP gene is transcribed into messenger RNA, which then directs synthesis of the protein.

These encapsulated translation systems exhibit a fundamental property of life: they use genetic information to synthesize a protein, but only a few specific proteins are produced, and everything else is left behind. To be truly alive, the protocells would need a DNA strand with genes for more than 200 different proteins and RNA species, including genes for a polymerase enzyme so that the DNA can be replicated. Enzymes that catalyze lipid synthesis must also be present, because the membrane boundary needs to grow. Transport proteins must be incorporated into the lipid bilayer; otherwise the vesicles have no access to external sources of nutrients and energy. A whole set of regulatory processes should also be in place, so that all this growth is coördinated. Finally, when the vesicles grow to approximately twice their original size, they need to divide into daughter cells that share the original genetic information.

It follows that even the simplest life today is astonishingly complex and could not have sprung into existence on the early Earth with a full complement of hundreds of genes. There must have been something simpler—a kind of scaffold life that was left behind in the evolutionary debris several billion years ago. Given all this, how likely is it that the ultimate promise of synthetic biology will be fulfilled—that an artificial version of a primitive living cell can be assembled? The best bet is probably a ribozyme that catalyzes its own complete synthesis from ATP, UTP, GTP, and CTP—the four nucleotide monomers of RNA—using genetic information encoded in its structure. If someone succeeds, we will have in hand the essential property that is lacking so far in artificial cell models: reproduction of the catalyst itself. Given such a ribozyme, we already know how to incorporate it into a system of lipid vesicles that can grow along with the ribozyme and allow nutrient nucleotides to enter the cell to support growth. The encapsulated ribozymes will have the capacity to evolve, as Bartel and Szostak demonstrated 15 years ago. In short, the system will be alive.

And then what happens? There will be headlines, of course; textbooks will be rewritten; and early in the morning someone will probably be awakened by a phone call from Stockholm. But after all the hullabaloo dies down; someone else will ask, "Well, so what?" That same question could have been asked when the double-helix structure of DNA was published in 1953. The magnitude of the discovery was not apparent until years later. I think that the first system of molecules capable of reproducing itself will also seem to be an academic exercise at first. But to put it in proper perspective, recall that food, antibiotics, oil, wood, methane, and hydrogen are produced by living cells resulting from more than three billion years of evolution. I think the next revolution in technology will begin when the synthetic functions of life can be performed by simplified versions of cells that are designed from blueprints rather than through evolution. TR

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REVIEWS

PERSONAL COMPUTING

Light, but not Lightweights

NETBOOKS ARE MORE THAN JUST CHEAP LAPTOPS.

By SIMSON GARFINKEL

For the cost of one night's stay in a New York hotel you can now buy a laptop that weighs 3.2 pounds, runs for more than seven hours with an extended battery, and is equally usable with Windows XP and the open-source Linux operating system. Pundits deride these "netbooks," saying they are good for little more than Web browsing and light editing. But I think these little machines are going to turn the personal-computer industry upside down.

The Asus Eee PC is widely seen as the first netbook to reach the U.S. market. Introduced in the fall of 2007, the Eee had a four-gigabyte solid-state disk (a "flash" drive) instead of a hard drive, and it ran Linux instead of Windows. Because it had a seven-inch screen and correspondingly tiny keyboard, industry experts predicted that Asus would be lucky to sell 300,000 units its first quarter in the market. It sold 350,000. Last year, roughly 10 million netbooks shipped, according to market research firm IDC.

Netbooks' success is due to more than their low price. Today's sleek, grown-up Eee PC 1000, available in multiple colors, has a 10-inch screen (1,024 by 600 pixels), a bigger keyboard, a full gigabyte of RAM, and a webcam, speaker, and mike. Asus sells different versions with solid-state drives up to 40 gigabytes or conventional hard drives with either 80 or 160 gigabytes. And now you can buy them with Linux or Windows XP—an operating system that runs just fine on this restricted little machine, thank you.

Netbooks are now available from Lenovo, Acer, Hewlett-Packard, Dell, and a number of smaller companies. Apple may even be working on one: last year the *New York Times*' John Markoff blogged that a search provider told him it had "spotted Web visits" of an Apple computer with a screen size somewhere between that of an iPhone and a MacBook.

LENOVO IDEAPAD S10E
$380

ACER ASPIRE ONE
$330

HP MINI 1000 MI
$280

DELL INSPIRON MINI 9
$275

ASUS EEE PC 1000
$400

Howard Locker, director of new technology at Lenovo, says that the right way to think about netbooks is as cheap laptops with processors and video cards four years out of date.

"From a processing and graphics viewpoint, they are from 2005," says Locker. But that's okay, he adds, because "the hardware has moved so rapidly beyond what people need, you can go with four-year-old technology and it's good enough" for most users.

Netbooks exist, says Locker, because no killer app has been developed that requires the full power of today's high-end notebook computers. He's half right.

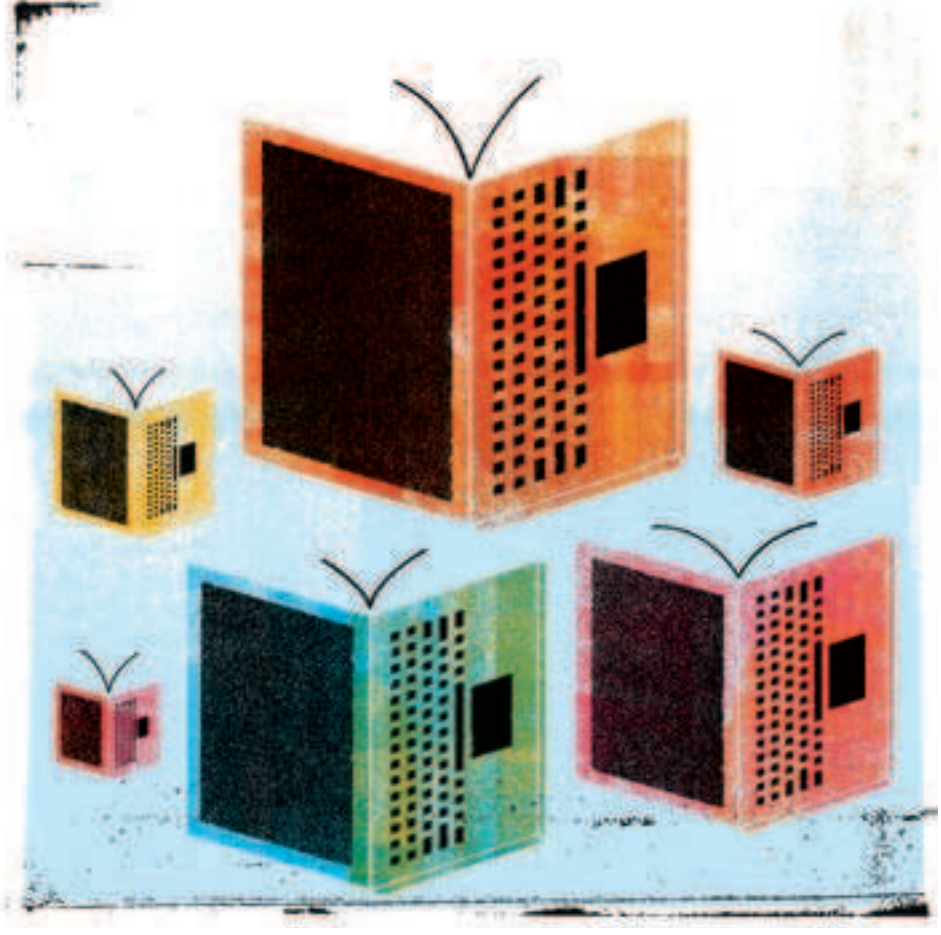
The fact is, many such killer apps with high-end computing requirements have been deployed since 2005. But they all run on the cloud-computing clusters used by companies such as Google, Facebook, and Twitter. To make the best use of those services, users want a take-it-anywhere platform. Lightness, not processing power, is a serious selling point. Hence the netbook's success.

POWER ON THE CHEAP

Except for the relatively small number of people doing high-performance gaming or streaming high-definition movies, today's computer users do not need all the power that top-of-the-line microprocessors can deliver. Companies like Intel and AMD know this. That's why they have spent much of the past four years innovating in different areas, such as power management and functional integration. Netbook technology emerged from those decisions.

Though today's netbook is indeed similar to a typical 2005 laptop in raw CPU and video performance—my 12-inch PowerBook had a gigahertz processor with 512 megabytes of RAM and a 60-gigabyte hard drive—it can do significantly more computing per watt of power than that 2005 machine. As a result, netbook vendors can use smaller, lighter battery packs, yet get more battery life than those older machines ever had.

These days most of the wait time experienced by PC users is caused by slow Internet connections or Web servers, not by slow client machines. As an experiment, I hooked up a Lenovo S10e to a 19-inch monitor and watched "The Man Trap," one of the original



Star Trek episodes, streamed from the CBS website. It took a good 30 seconds for the Flash-based player to download over my pathetic DSL connection, but as soon as the playback started, it was flawless.

So not only are netbooks cheap, but they are powerful enough for ordinary computing. The main reason the engineers and professionals I've spoken with have purchased them, though, is the combination of cost, weight, and battery life. That's the beauty of the netbook: these criteria are mutually supporting.

Netbooks also do a fine job running traditional productivity applications such as Microsoft Office. Every netbook running Windows XP that I examined for this article came with a complete copy of Office 2007 installed and ready to go.

Just because a $300 netbook *will* run Microsoft Office, however, doesn't mean that it *should*. That preinstalled copy is just a 60-day trial; to use it longer requires buying an activation key from Microsoft's online store for between $240 and $400. I find it hard to justify spending more on Office than on the netbook itself—particularly when the free alternatives, Open Office and Google Docs, keep getting better. The netbook's low, low price can't be good for sales of Microsoft Office—or for sales of Windows.

Another software vendor bound to be troubled by the netbook's price is Apple. Over the past few months, more than a dozen websites have popped up offering instructions on how to get Apple's Leopard operating system to run on these low-cost laptops. Apple is not pleased; it even forced Wired.com to take down a video showing how to install OSX on an MSI Wind netbook.

The problem here is that even though Apple sells Leopard in shrink-wrapped boxes for a little more than $100, the software is licensed for use only on Apple hardware. Some feel that Apple has no business controlling its software in this way, for the same reason that booksellers in the United States are not allowed to use "license agreements" that prohibit their customers from lending or reselling used books—a principle technically known as the "first sale" doctrine. Ultimately, questions about the application of this doctrine to software will be resolved in court—probably several courts.

I didn't care about this issue when Apple's laptops cost only $200 more than the competition's. But when the MSI Wind can be had for almost $1,500 less than the Macbook Air, it becomes upsetting. Many people want to run MacOS but don't want to pay the premium for Apple hardware. Now they have a choice, albeit one of questionable legality.

TROUBLE IN A MINOR KEY

The netbooks' small size and light weight make them much more portable than traditional laptops. I often don't carry my 15-inch MacBook Pro, simply because it weighs seven pounds, including power supply and spare battery. But I walked around with the Acer Aspire One in my backpack for *three days* without even realizing it: I'd loaded up the machine, gone off to a coffee shop, and then simply forgotten that it was in there.

But what about usability? I decided to take a rough survey. Not surprisingly, the main complaint concerned netbooks' cramped keyboards and nonstandard key positions. I've had a hard time with the placement of the shift key on the Lenovo—I keep pressing the up arrow by accident. And keyboard complaints dominate the negative comments I've seen in online forums. Similarly, the netbook users I've accosted with queries at coffee shops and conferences agree that the keyboards are annoying. Yet most users insist that they adjusted to the size and layout after only a few hours.

Those who demand a large keyboard should take a serious look at the HP Mini 1000. This machine has bigger keys arranged in a more traditional layout than the other netbooks: I could type on the 1000 with my eyes closed and not make an error.

Since most netbook vendors also have successful lines of full-size laptops, I suspect that they may have purposely kept their netbook keyboards small and cramped in an effort to differentiate the netbooks from their ultralight laptops in the $900-to-$2,000 range. But such efforts at market segmentation won't last, as the Eee PC 1000 and Mini 1000 demonstrate. I expect larger keyboards to show up on these netbooks over the next year, since adding an inch to a

keyboard adds little to the cost while making the system much more usable.

My loose survey did bring one surprise: a lack of complaints about the netbooks' small screens. It's true that a screen just 600 pixels high is quickly consumed by the menu and button bars of most Microsoft applications. On the other hand, most applications can be reconfigured to make more judicious use of the vertical real estate. The netbooks' limited height is not a problem with websites, since netbooks scroll fast.

Finally, since netbooks have USB inputs and standard video outputs, small keyboards and screens are really an issue only when you're on the road. At home you can use an external keyboard, mouse, and display. Netbooks are bound to make dockable laptops much more appealing to home users than they have been until now.

DISPOSABLE AND DISRUPTIVE

Netbooks are so cheap it's not far-fetched to imagine that a person might want to buy a new one each year.

Indeed, the netbook's price poses yet another, albeit indirect, danger to Microsoft. Aware of such a low-cost alternative, Windows users will find it hard to justify spending hours downloading software, installing applications, and customizing preferences every time they buy a new machine. For that reason, expect netbooks to live up to their name and accelerate the trend of cloud computing, whereby software and services are accessed over the Web. Lenovo even offers a Linux-based quick-starting shell that lets you get on the Internet less than 10 seconds after turning on the machine.

Netbooks might expand the U.S. laptop market to people who could never before afford one. But they are sure also to cannibalize today's laptop market, slashing profits for both hardware and software makers. These machines are probably bad for Microsoft, Intel, and Apple. But they're going to be great for Google, Facebook, and Twitter. TR

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HEALTH CARE

A Lifelike Prosthetic Arm

THANKS TO A NEW SURGICAL PROCEDURE, ARM AMPUTEES CAN INTUITIVELY CONTROL A BIONIC LIMB FOR THE FIRST TIME.

By MICHAEL ROSENWALD

People who have lost an arm have not traditionally had much hope of ever regaining meaningful function. Prosthetic arms have been controlled in a rudimentary way, by transforming residual shoulder movements or muscle signals into the simplest movement commands. These artificial arms cannot do two things at once, much less three or four. Amputees often toss them in the closet out of sheer frustration, somewhat stung by the fact that leg amputees have far better products available to them.

TARGETED MUSCLE REINNERVATION

But the situation is starting to change, thanks to a team led by Todd Kuiken, director of the Rehabilitation Institute of Chicago's Center for Bionic Medicine. Kuiken has developed a novel surgical technique that, when paired with both motorized prosthetic arms already on the market and experimental bionic arms developed through a Defense Advanced Research Projects Agency (DARPA) program, affords amputees a remarkable degree of dexterity. Claudia Mitchell, who lost her arm in a motorcycle wreck in 2004, remembers putting on a prosthesis after undergoing Kuiken's procedure and seeing it work for the first time: "You could not wipe that grin off of my face. I can now iron a shirt again like nobody's business." Mitchell has become a hit at parties. "People can't believe how this thing works," she says. "They want to see me do things with it."

The device is activated by commands from surviving arm nerves that have been transplanted and rewired to muscles elsewhere—typically, as in Mitchell's case, in the chest. The nerves send electrical signals to control the prosthetic arm, with results so natural that observers often don't realize the arm is bionic until they listen closely for the sound of whirring motors. Called targeted muscle reinnervation, the procedure is unique because it permits intuitive control over the robotic limb. After about six months of healing, patients can move the arm merely by thinking about what they want it to do, just as they once did with their real arms. Tell Mitchell "Bend your arm," and the muscles in her chest flinch instantaneously—a most peculiar sight. But she is not thinking about moving her chest muscles. Rather, she is thinking about bending her arm, and that thought moves the chest muscles to make the robotic arm do her bidding.

Kuiken recently published promising test results in the *Journal of the American Medical Association*, showing that five patients told to perform 10 different arm movements with a virtual prosthesis could do so almost as readily as non-amputees in a control group: their response time was less than a quarter of a second longer. (The virtual prosthesis allows scientists to more easily figure out the speed and level of control that can be gleaned from muscle signals. Researchers performed similar experiments with mechanical arms.) In an accompanying editorial, the pioneering biomedical engineer Gerald Loeb wrote, "The speed as well as the accuracy of the movements represent substantial improvements over previous systems. Even more important, however, is the ease with which patients learned to perform tasks requiring coordinated motion in more than one joint." He concluded, "With increasing functional capabilities, patients with upper-extremity amputations may derive exceptional benefit from

prosthetic arms, just as legions of patients with lower-extremity amputations now lead remarkably normal and even athletic lives." (Leg prostheses have been further along in development because there is a bigger market for them: 90 percent of amputees have lost lower limbs. Also, legs don't require as much dexterity as arms.)

The journey from initial consultation in Chicago to full functionality—say, the ability to slice a lemon with the prosthetic hand while holding it with a natural hand—often takes a year or longer. Patients first undergo a two-hour surgery performed by Greg Dumanian, a Chicago plastic and hand surgeon who has worked closely with Kuiken in developing the procedure. Dumanian identifies the surviving portion of the nerves that previously conducted electrical signals from the spinal cord to the lost limb; then he transfers them to muscles in the chest or upper arm. The nerve that would normally trigger the hand to close might be transferred to part of the chest muscle, for example. (The exact procedure varies according to the patient's injuries.) When the robotic arm is in place, an electrode on the chest detects contractions in this muscle and sends the signal to the prosthesis. The prosthesis is programmed to interpret that signal as a command to close the hand, and the action typically takes place less than half a second after the chest muscle moves.

The experimental bionic arms are also programmed with pattern recognition algorithms to decipher the rapid series of nerve signals that govern hand and wrist motions. The more than 30 patients who have had the procedure report that they are easily able to slice hot peppers, open a bag of flour, put on a belt, operate a tape measure, or remove a new tennis ball from a container.

Among several experimental approaches to improving prosthetic arms, including transferring nerves directly to a prosthesis and decoding movement signals directly from the brain, Kuiken's technique is the one that has made the most progress. The former has yet to be tested in humans, and the latter is currently considered too dangerous for most patients, since it requires brain surgery. Kuiken says he views targeted reinnervation as a quicker, more practical way of restoring crucial functions. (His approach won't help quadriplegics, however, because the nerves need to be intact for the procedure to work.) So far, the procedure is performed only at Kuiken's rehab center; in ongoing studies, the center is offering it to any patient for whom it's deemed medically appropriate.

A BIONIC ARM After undergoing a novel surgical procedure, Claudia Mitchell can control a prosthetic arm much as she once controlled her real arm, performing complex movements such as picking up small objects and dropping them into a cup.

Advanced though it is, the experimental prosthetic is still missing a major function: sensation. If Mitchell were to place her bionic hand on a hot pan, she would have no way of knowing its temperature. Giving the prosthetic sensory capabilities similar to those of a real limb is more complicated than restoring movement. But it's not impossible. While Kuiken's procedure focuses on moving motor nerves, which conduct nerve signals from the brain to the muscles, it appears that sensory nerves, which carry signals from the skin to the brain, are affected as well. Patients, including Mitchell, have reported that when certain areas of their rewired chest muscles are touched, they feel as if their missing hand is being touched. Place an ice cube on the chest, and a phantom hand gets cold.

Kuiken, Loeb, and others are studying ways for the bionic arm to make use of this sensory information. For starters, they'll need sensors that can stand up well to moisture, heat, and the other physical eventualities of daily living. They'll then need to deliver that sensory information to the wearer.

But what's clear now is that for the first time, a useful prosthetic arm is in sight. "We're not trying to make a bionic person who can leap tall buildings and pick up cars," Kuiken says. "We're trying to make something that restores a fraction of the incredible function and power and efficiency of a human limb." For arm amputees like Claudia Mitchell, that means getting a chance that leg amputees have had for years. TR

MICHAEL ROSENWALD IS A STAFF WRITER AT THE *WASHINGTON POST*.

IMAGES COURTESY OF THE REHABILITATION INSTITUTE OF CHICAGO AND DEKA RESEARCH

LIE DETECTION

Telling

TO A FEW HUMAN EXPERTS, OUR FACES—AND DEEPEST EMOTIONS—ARE OPEN BOOKS. NOW COMPUTER TECHNOLOGY AUTOMATES THOSE EXPERTS' ABILITIES.

By MARK WILLIAMS

In the late 1960s, Paul Ekman—then a young psychology professor at the University of California, San Francisco, School of Medicine and just commencing his life's work—filled a San Francisco Victorian with a library of films showing 40 psychiatric patients' faces as they were interviewed. Ekman, who is now a leading figure in his profession, wanted to know whether he could isolate facial expressions to help diagnose mental disorders. A woman named Mary, who had attempted suicide three times before, smiled and spoke cheerily on her tape. As it happened, she was angling for a weekend pass—so that she could go home and kill herself.

"Mary was how I first discovered microexpressions," Ekman told me when I caught up with him on the set of *Lie to Me*, the Fox television drama inspired by his decades of research into how facial expressions, gestures, and other nonverbal behaviors reveal our emotions and—most pertinently—our deceptions. "Some young psychiatrists I was teaching asked whether I could help identify when a suicidal patient was telling the truth or lying about improving," he said. "Some of their patients had left the hospital and killed themselves within an hour. Mary, however, had confessed before she left that she'd been lying during a [previous] interview I'd filmed. Looking at the film, I couldn't see any evidence. So I went through it frame by frame for a week, and these microexpressions showed up—two instances, each a 25th of a second, out of 12 minutes."

In Mary's case, her features had fleetingly exhibited despair when the interviewing doctor asked about her plans. Ekman learned that the human subjects he studied betrayed their emotional state through microexpressions, however much they tried to suppress them. He identified 46 facial-muscle movements that, across cultures, signal such basic emotions as fear, distrust, and distress.

"What I didn't know at the beginning," Ekman told me, "was you could train people to recognize these microexpressions in real time." He developed the Facial Action Coding System, or FACS, in the 1970s as an exhaustive taxonomy of all facial expressions, including these telltale muscle behaviors. Since then, trained FACS users have generally demonstrated better than a 75 percent success rate in reading faces. *Lie to Me*—which stars the estimable Tim Roth as Dr. Cal Lightman, the character based on Ekman—is very average entertainment in the genre of Fox's great success *House*, where a maverick expert solves cases that establishment types cannot. In reality, however, a lot of FACS users are establishment types—cops, FBI agents, members of the U.S. Secret Service.

COMPUTER EXPRESSION RECOGNITION TOOLBOX (CERT)
mplab.ucsd.edu/grants/project1/research/Fully-Auto-FACS-Coding.html

LIE TO ME
Fox
www.fox.com/lietome/

It requires no innate gift to apply Ekman's research in practice. "You could go online now [www.mettonline.com] and learn the microexpression recognition, which is one part, in an hour," Ekman says. With practice, most of us could decode these fleeting expressions in real time. "Initially, everybody believes they'll never do it," he says. "By the end, they're asking, 'Are you slowing these things down?' We're not, but your eyes have learned to see them."

Other studies bear out Ekman's claims. In research conducted in 2006, neuroscientist Tamara Russell of the University of London's King's College showed that an hour of microexpression training enabled people with schizophrenia to identify facial expressions as accurately as healthy people.

Some, however, are much better than others at reading microexpressions. Ekman's University of San Francisco colleague Maureen O'Sullivan has tested 20,000-odd folks over two decades and identified 50 individuals among that number who consistently demonstrate over 80 percent accuracy in detecting when others are lying, with a very few approaching perfect accuracy. Clearly, some specific, optimal set of capabilities underlies these rare individuals' success.

Since trained FACS experts generally replay footage for three hours in order to analyze just a single minute of a subject's facial twitches and blinks on video, it made sense to ask whether a computer system could automate the process of microexpression analysis and match O'Sullivan's human "wizards." Ekman first considered the challenge in the late 1980s. On a sabbatical in London, he visited Brunel College, where an engineer who had developed one of the first parallel-processing computers was training an artificial neural network to recognize terrorists. The engineer's problem was that subjects' varied facial expressions made it difficult for his system to recognize their identities, while Ekman's difficulty tended to be the reverse: he needed to disregard his subjects' individual physiognomies to recognize the emotions revealed by their expressions. So the two men worked together. "Within three days, we taught the machine to recognize three different emotions on different people," he says. "Back in the U.S., I wrote up a grant proposal for the NIH, who turned it down, claiming parallel-processing computers didn't exist." Ekman expressed his frustration to a friend who was a Nobel Prize–winning physicist; the friend contacted Terry Sejnowski, the cross-disciplinary eminence of computational

LIE DETECTION IS TRICKY Is Richard Nixon, here interviewed by David Frost in 1977, on the level? Research finds that "microexpressions" reveal our basic emotions, whether we like it or not.

ASSOCIATED PRESS

neurobiology at the Salk Institute, whose lab had the necessary computers. Ekman and Sejnowski teamed up and got the grant.

Mark Frank, a former postdoctoral student of Ekman's and now a professor at the University at Buffalo, in New York, has had the greatest success automating FACS. Frank, working out of Buffalo's Center for Unified Biometrics and Sensors, has worked with a group of computer scientists at the University of California, San Diego—mostly former students of Sejnowski's—to turn FACS into a technology called the Computer Expression Recognition Toolbox (CERT). I asked him how the project was going.

"We've done it," Frank told me. "We have a system that operates in real time. In terms of machine learning, we had to give the machines good audiovisual material with real emotions and expressions. Then it's just a matter of training, testing, training, testing." CERT works about as well as a human expert, he says, but it's a little faster.

A technology that accurately detects people's true emotions possesses tremendous political, social, and commercial potential. What if political commentators had applied it to footage of last year's U.S. presidential debates, for instance, to reveal if McCain or Obama was lying? Or if lawyers used it to analyze video depositions presented during court trials to determine whether a witness had lied, a finding that could be cited as evidence? Indeed, since the technology mines ordinary video, it might be commodified as a cheap Web service so everybody could use it: people might record job interviews, business negotiations, prenuptial-agreement signings, wedding ceremonies, or any other kind of civil transaction, with an eye toward reviewing them to ascertain the good faith of those involved. "You wonder what you do when the cat comes out of the bag," Frank says. "And can you get it back in?"

The argument for admitting such evidence in court seems straightforward. To be admissible, a technology must satisfy one of two legal standards; the *Daubert* test (from the 1993 U.S. Supreme Court case *Daubert v. Merrell Dow Pharmaceuticals*) is the one used in most jurisdictions. "*Daubert* requires that scientific testimony must qualify as reliable 'scientific knowledge,'" says Edward Imwinkelried, a law professor at the University of California, Davis, who is an expert on the admissibility of scientific evidence. "The Supreme Court defines 'scientific knowledge' as knowledge validated by a specific methodology, which it described in classic terms as, firstly, the formulation of an hypothesis and, secondly, the subsequent controlled experimentation or systematic field observation to verify or falsify the hypothesis." Given FACS's three decades of acceptance and CERT's record of accuracy, automated facial-expression analysis might well meet those criteria.

Making this argument, however, would require the support of expert witnesses like Frank or Ekman, and that's not forthcoming. Frank, for instance, supports CERT's use by the U.S. government for purposes of national security—it may happen by 2011, he guesses—but he doesn't want to see the technology spread much further: "Though we get a call every two weeks from people wanting to make the big bucks by marketing this as lie detection, I'm proud that nobody involved in the science has thus far gone beyond what it supports."

What the science confirms is that both FACS and CERTS can reveal much of any human subject's real emotions, but those results must be construed intelligently—especially in the context of detecting deception. Otherwise, Ekman summed up, users risk what he calls "Othello's error": "Othello read Desdemona's fear accurately. But he didn't recognize that the fear of being disbelieved is just like the fear of being caught. Yes, our faces reveal what emotions we're experiencing, if you can read the signs. What our faces don't necessarily reveal is what triggered that emotion." If you don't know that, interpretation can go far astray. "Rule out all the possible explanations before you conclude that what you're seeing is a sign of lying about a criminal act," Ekman warns. "Because very often, it's not." TR

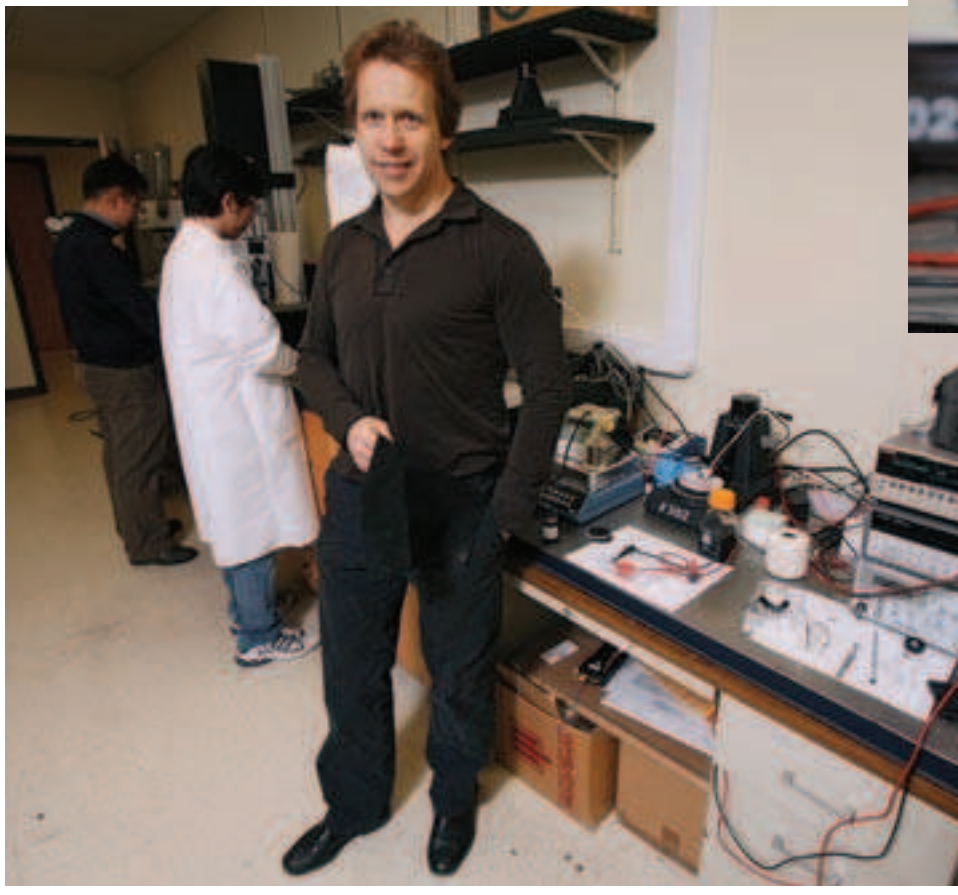
MARK WILLIAMS IS A CONTRIBUTING EDITOR TO *TECHNOLOGY REVIEW*.

DEMO

Nanotubes Come into Fashion

TEXTILES COATED WITH CARBON NANOTUBES FORM ELECTRONIC SENSORS THAT LOOK AND FEEL LIKE ORDINARY COTTON.

By KATHERINE BOURZAC



FABRIZIO COSTANTINI

Elegance is as important in scientific design as it is in art and architecture, chemical engineer Nicholas Kotov believes. Sitting in his austere office at the University of Michigan, in Ann Arbor, he shows off a swatch of black cotton; in heft and feel it's similar to a soft, lightweight dress shirt. But Kotov has transformed the fabric into a biosensor and an electrical conductor simply by dipping it into a solution of carbon nanotubes, antibodies, and a polymer.

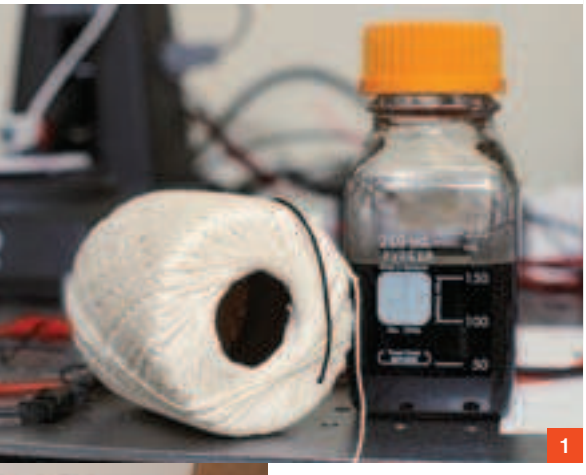
Individual, well-formed carbon nanotubes are highly conductive, which makes them promising for applications such as battery electrodes and microprocessors. If molecules such as antibodies are anchored to their surface, they can also serve as very sensitive chemical detectors: when an antibody binds to its target, the nanutobe's electrical properties are measurably altered. But nanotubes tend to clump together, which prevents them from functioning individually. That seriously degrades their electronic properties, says Kotov.

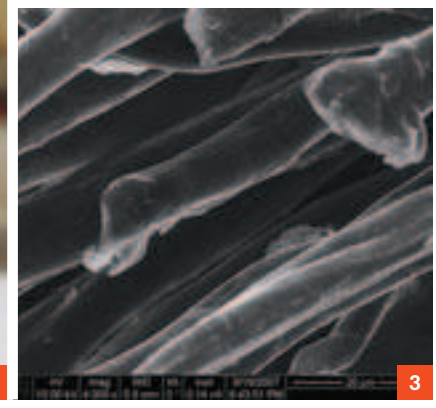
There are ways around this problem: nanotubes can be painstakingly laid down, one by one, using methods that involve days of solution processing followed by photolithography, or the tubes can be sprayed onto a flat surface in alternate layers with a conductive polymer, which prevents clumping. But Kotov found that this type of layer-by-layer assembly can be further simplified for a complex three-dimensional surface such as a cotton thread: the tangle of fibers provides a structural template that allows him to simply dip the thread into a solution containing both the polymer and the tubes. Glued to the thread by the polymer, the nanotubes form a net with good electrical properties, the tubes overlapping but well spaced.

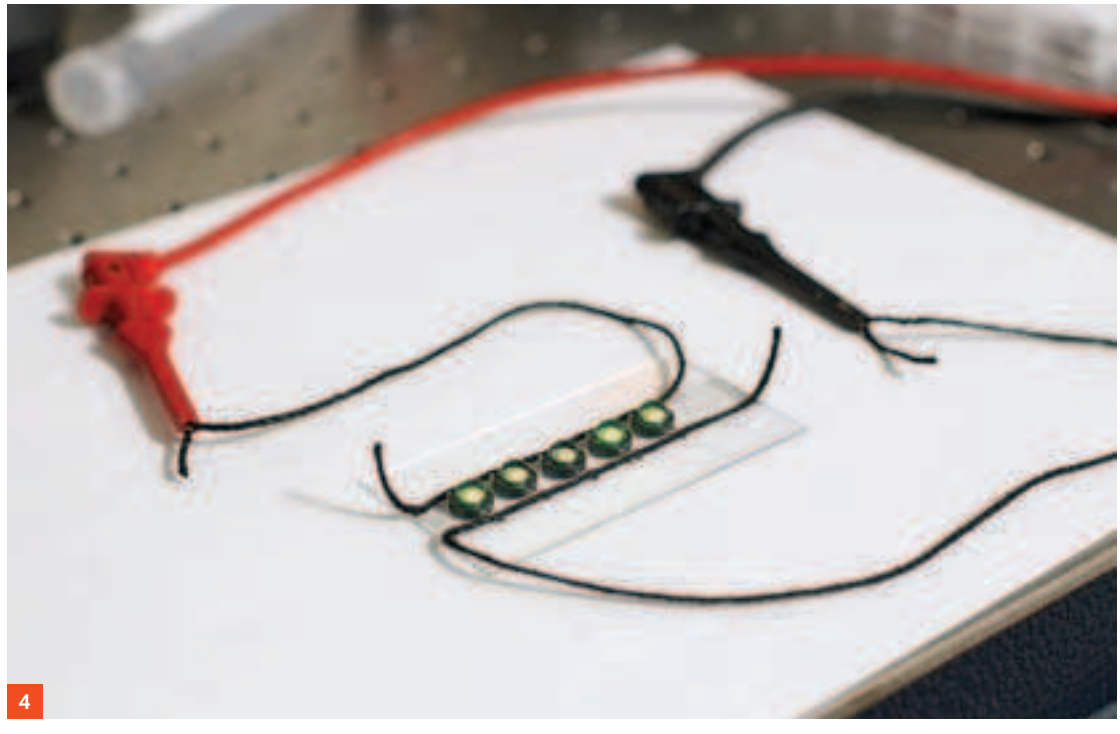
The method results in a sleek, powerful, and much more wearable alternative to complex intelligent textiles that incorporate heavy, bulky optical fibers or corrosion-prone metal wires. While Kotov is exploring a number of possible applications for these textiles, the most important, he says, would be as biosensors to keep people safe. They could be used to spot blood loss in soldiers on remote patrols or to detect airborne allergens or pathogens such as influenza. And the threads are cheap and sensitive enough for possible use in factories or stores, or even in the home—for example, to test an iffy batch of peanut butter for toxins.

A QUICK DIP

In Kotov's lab, graduate student Jian Zhu mixes commercially available single-walled nanotubes and a polymer called Nafion into ethanol, which prevents the components from sticking together. The Nafion glues the nanotubes to the cotton, but that's not all it does. Nafion, a long, conductive molecule composed primarily of carbon, acts like a tiny spring, allowing each nanotube some







measure of independent movement. This mechanical property, which is critical for biosensing, also allows the cotton to maintain its softness and give: you wouldn't want to wear a shirt coated in stiff epoxy.

Zhu snips a length of ordinary cotton thread from a spool and uses a pair of tweezers to submerge it in the inky-black solution. After it sits for two minutes, he fishes out the thread and uses a binder clip to hang it up to dry inside a lab hood, a process that can be shortened to only a few minutes with a hair dryer. The electrical resistance of the thread is optimized, Kotov has found, when it has been dipped about 10 times.

In the group's student office, Zhu demonstrates the electronic properties of a finished nanotube thread, which is indistinguishable from ordinary black cotton. He attaches it to the electrical contacts on a white light-emitting diode using ordinary solder, then draws the ends of the thread through the positive and negative clips on a power source. He turns the power source up to three volts, and the light shines brightly.

SIMPLE ADDITION

The tiny light is not, at first glance, very impressive. But three volts is enough power for the threads to carry out functions such

Left: Nicholas Kotov in his lab at the University of Michigan, where he makes carbon-nanotube-treated textiles like the one in his right hand.
1. The process starts with ordinary cotton thread and an ethanol-based solution of carbon nanotubes and the polymer Nafion.
2. Jian Zhu pulls a cotton thread out of the nanotube solution, where it's been soaking for about two minutes. Zhu will allow the thread to dry and then repeat the process about nine times to maximize the thread's electrical properties.
3. Visible in this image from a scanning electron microscope, the microscale fibers that make up a cotton thread provide a structural template for the nanotubes to adhere to.
4. Treated threads are attached to electrodes on five light-emitting diodes and to a power source (by the red and black clips). The threads carry enough current to light all five LEDs.

5. Zhu holds small patches of cotton cloth treated with the nanotube-Nafion solution. The dipping technique used on individual threads can also turn whole cloth into an electronic textile.
6. When antibodies to human albumin are added to the nanotube solution, the treated threads can sensitively detect blood. In a solution containing a small amount of human blood (dye added for visual emphasis), the thread becomes much less resistant to the flow of electrical current. A solution with just a tiny amount of albumin in it causes the thread's resistance to drop significantly.

as biosensing. Kotov can turn the nanotube textiles into sensors simply by including antibodies in the initial ethanol solution. Because antibodies are sensitive to heat, the researchers let the material air dry instead of using a hair dryer; otherwise, the process is the same. The addition of the antibodies causes the fiber's resistance to vary with the concentration of the antibody's target molecule. Zhu takes a thread treated with a solution containing the antibody to the human version of the blood protein albumin and hooks it up to a multimeter, which supplies steady voltage to the thread and allows him to watch how its resistance changes. As he dunks the fiber into a dilute solution of blood, the thread's resistance drops from 60 kiloohms to 20.

When the cotton is dipped into a solution of nanotubes, Nafion, and antibodies, the antibodies are physically trapped at intersections in the nanotube nets. When blood molecules adhere to the treated fabric, these antibodies attach to the albumin in plasma. The albumin-antibody complex, which is very soluble in blood, detaches from the nanotubes, allowing them to move closer together. Because current travels between nanotubes by means of "quantum tunneling," essentially hopping from tube to tube, a small change in the distance between them "can lead to tremendous changes in resistance," explains Kotov. The decrease in resistance that results when the antibodies detach from the thread is a more reliable measurement of albumin concentration than a decrease in conductivity would be. Reduced conductivity might be caused by dirt or other contaminants, but a decrease in resistance is a sign of just one thing: albumin, and thus spilled blood. Connected to a PDA capable of interpreting and even transmitting the results, clothing made from fabric treated this way could "generate a distress signal if, for instance, you're unconscious," says Kotov.

Using antibodies also makes this detection mechanism very specific: when the fabric is exposed to bovine blood, which contains a slightly different form of albumin, its resistance doesn't change. Treated with antibodies against other proteins, such fabrics might help doctors monitor hospital patients for infections or warn asthmatics of allergens, Kotov says. And the method is so simple, sensitive, and potentially cheap that fiber-based nanotube sensors might even be used in place of emerging chip-based detectors to test blood samples for signs of diseases such as cancer.

Kotov's sensors, while very reliable, are not reusable: once the antibodies detach from the nanotubes, they're washed away, so the fabric can't detect proteins a second time. Kotov says the fabrics should be inexpensive enough for single use. He's also working on reusable versions, changing the chemistry so that the antibodies release their targets after detection and remain in the fabric.

Kotov is already working with Nico Technologies to develop garments made from the textiles for undisclosed military and civilian applications. However, he notes, future garments might include different types of coated thread, each treated for a different function. "You need just a single [nanotube-treated] thread in a garment," he says, "and all the fundamental advances of nanotechnology are there." TR

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FROM THE LABS

BIOMEDICINE

Mind Reading

BRAIN IMAGING CAN REVEAL WHAT A PERSON IS THINKING

SOURCE: "DECODING REVEALS THE CONTENTS OF VISUAL WORKING MEMORY IN EARLY VISUAL AREAS"
Stephenie A. Harrison and Frank Tong
Nature 458: 632–635

Results: By analyzing data collected with functional magnetic resonance imaging (fMRI), researchers identified with 83 percent accuracy which of two images a person was remembering.

Why it matters: Previous research has shown that fMRI can reveal which of a number of pictures a person is looking at. But the new study is unique in identifying what the subject viewed before the brain imaging took place. The study also sheds light on where in the brain visual working memories are stored.

Methods: Subjects were briefly shown two successive images of a grating oriented at different angles. They were asked to remember one of the images as an fMRI scanner monitored blood flow in the brain, a proxy for brain activity. Scientists then used specially designed algorithms—derived from previous brain scans of each person—to search for activity patterns that indicated which image the person was thinking of, several seconds after the image itself had disappeared.

Next steps: The researchers are now testing the technique with more-complex visual patterns and exploring ways of using it to gather more information about what people are actively remembering.

Fighting the Flu

NEWLY MADE ANTIBODIES PROTECT AGAINST MULTIPLE VARIETIES OF FLU

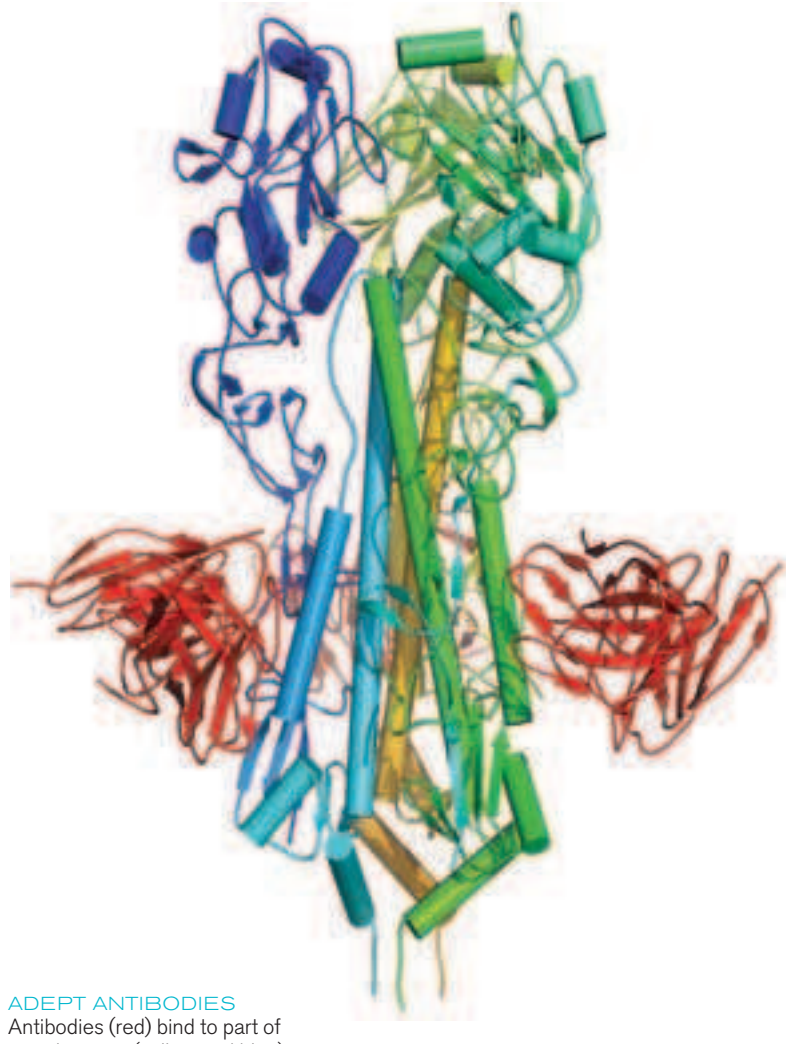
SOURCE: "STRUCTURAL AND FUNCTIONAL BASES FOR BROAD-SPECTRUM NEUTRALIZATION OF AVIAN AND HUMAN INFLUENZA A VIRUSES"
Jianhua Sui et al.
Nature Structural and Molecular Biology 16: 265–273

Results: Scientists have developed antibody proteins that can neutralize multiple strains of the influenza virus, including common seasonal strains, the deadly H5N1 bird flu, and the virus behind the 1918 epidemic.

Why it matters: Most flu vaccines are effective against only a specific strain of flu; they must be reformulated every year, because they target a part of the virus that constantly mutates to produce new seasonal strains. But the new antibodies target a part of the virus that is common to different strains, so they appear to be broadly effective.

Methods: Scientists first screened billions of antibodies and found a small group that protected against different types of bird flu. Three of these had broad neutralizing abilities when tested in cells and in mice. By looking at the structure of the successful antibodies and analyzing the way they bind to viruses, the scientists identified a part of a protein on the virus's surface that is shared by different strains of influenza.

Next steps: Researchers will test the antibodies in ferrets, the "gold standard" animal model for influenza, and then develop clinical-grade versions for human testing.



ADEPT ANTIBODIES
Antibodies (red) bind to part of a viral protein (yellow and blue).

WILLIAM C. HWANG

INFORMATION TECHNOLOGY

Smarter E-Mail

PROTOTYPE DRAWS DATA FROM MULTIPLE SOURCES TO FIGURE OUT WHERE TO SEND MESSAGES

SOURCE: "SEMANTIC EMAIL ADDRESSING: THE SEMANTIC WEB KILLER APP?"
Michael Genesereth et al.
IEEE Internet Computing 13 (1): 48–55

Results: Researchers at Stanford University have developed a prototype system that allows people to send e-mail to individuals or groups without knowing the recipients' e-mail addresses or names. The system scours databases and websites to find addresses for people who fit selected criteria, then sends messages to those addresses.

Why it matters: The system would make it easier for e-mail to reach the correct destination, even when the sender isn't sure what that destination is. It would allow a person to send a message to "Bob Jones," say, even if Bob Jones changed jobs and has a new address—or to direct an e-mail to "head of the marketing department," even if the person holding that position has changed. It could also be used to find several people at once who fit certain criteria.

Methods: The researchers developed software that analyzes requests, such as "Professors who went to Harvard before 1970." Since data needed to fulfill this request will come from various databases that categorize information in different ways ("professors," "Harvard," and so on), the researchers also devised an intermediary program. That program translates these requests into terms that will be understood by the databases being queried. For example, a request for Harvard might be directed to a number of database categories, such as "college," "institute," and "university."

Next steps: The system, which currently gleans addresses from a specific set of university and research-institute databases, must be adapted to work with more databases. It can also be used to gather e-mails from websites that use a standard framework for categorizing information. And the system could be used to filter spam. For example, someone could choose to accept e-mail only from "researchers studying the semantic Web," and the system would identify addresses of those people and allow messages from them.

Improved Memory

NEW ALGORITHMS DOUBLE FLASH CAPACITY WITHOUT SHRINKING TRANSISTOR SIZE

SOURCE: "A 5.6 MB/S 64 GB 4B/CELL NAND FLASH MEMORY IN 43NM CMOS"
Cuong Trinh et al.
2009 IEEE International Solid-State Circuits Conference, February 10, 2009, San Francisco, CA

Results: Researchers at Toshiba and SanDisk, a maker of flash memory devices in Milpitas, CA, have built a 64-gigabit chip that holds four bits of data per memory cell, twice as much as the cells in conventional chips.

Why it matters: To increase the amount of data that can be stored in memory chips, engineers typically shrink the transistors that make up the individual memory cells. However, as transistors get smaller, their reliability tends to decrease because they generate more heat and leak more electrical current. While SanDisk researchers are still exploring ways to make transistors smaller without compromising reliability, the new approach makes it possible to store more data without shrinking transistors.

Methods: In conventional flash memory, a transistor stores two bits of data, each defined by a distinct voltage level. A variation of the technology can store four bits per transistor, but this requires more finely tuned voltage levels that can be disrupted by extreme voltage differences between transistors, effectively erasing the data. The SanDisk researchers wrote an algorithm that controls the way data is written to the chip so that the voltage differences between neighboring transistors are kept to a minimum.

Next steps: The company expects its chips to go into production within the first half of 2009. Future chips may

COMPACT MEMORY A micrograph shows the two 32-gigabit sections of a new flash memory chip.

COURTESY OF SANDISK

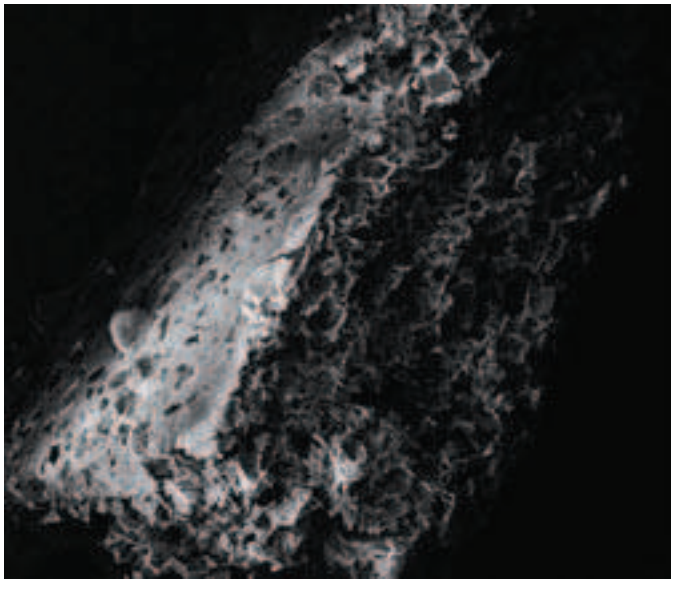
use a similar principle, but since the electrical characteristics of transistors will change as smaller ones are developed, applying this approach to new generations of memory chips will require new algorithms that take these changes into account.

MATERIALS

Cell Programmer

A POLYMER IMPLANT SIGNALS CELLS TO COMBAT CANCER

SOURCE: "INFECTION-MIMICKING MATERIALS TO PROGRAM DENDRITIC CELLS *IN SITU*"
David Mooney et al.
Nature Materials 8: 151–158



CELL TRAINER Immune cells attracted to nooks in this porous, biodegradable polymer implant are stimulated to attack cancer.

Results: A new implant attracts immune cells and exposes them to molecules that stimulate them to attack cancerous tumors. When tested in mice that normally die of cancer within 25 days, the implants allowed 90 percent of the mice to survive. Similar experimental therapies based on transplanting immune cells are only about 60 percent effective.

Why it matters: The implants could eventually be used to treat human cancers that don't respond to other therapies, and they could also be used to treat immune disorders such as type 1 diabetes and arthritis. Other approaches that involve stimulating immune cells haven't proved successful in clinical trials. Those techniques require the cells to be removed from the body and then reimplanted; many are damaged in the process and die, while survivors often fail to trigger attacks on cancerous tumors. The new implant stimulates cells inside the body, without subjecting them to stressful procedures.

Methods: The spongelike implant is made of a biodegradable polymer that releases chemical signals called cytokines. In mice with melanoma, these signals attract immune cells called dendritic cells to the nooks and crannies of the implant. There the cells are exposed to a cancer antigen that stimulates them to attack tumors. When tissues from the mice were analyzed, the researchers found that dendritic cells had migrated to the lymph nodes and activated other immune cells, and the animals' tumors had shrunk.

Next steps: Before proceeding to clinical trials, the implants must pass safety tests in large animals. Long-term studies will then establish whether the immune system will attack cancer that may recur years after the implant has degraded.

Ethanol Fuel Cell

A NEW CATALYST COULD MAKE THE TECHNOLOGY USABLE IN PORTABLE ELECTRONICS

SOURCE: "TERNARY PT/RH/SNO2 ELECTROCATALYSTS FOR OXIDIZING ETHANOL TO CO2"
Radoslav Adzic et al.
Nature Materials 8: 325–330

Results: A new catalyst efficiently breaks the strong carbon-carbon bond at the center of ethanol molecules, converting ethanol to carbon dioxide in a process that releases protons and electrons. It generates electrical currents 100 times greater than those produced with other catalysts that oxidize ethanol.

Why it matters: Ethanol-powered fuel cells based on the catalyst could open the way for portable electronics that can be refueled faster than battery-powered devices can be recharged. The technology would also be safer than portable fuel cells that use toxic methanol. Previous catalysts used to free electrons from ethanol were inefficient: either they used a great deal of energy to break the carbon-carbon bond or they broke only the molecule's weaker bonds, releasing just a few electrons per molecule. The new catalyst efficiently frees 12 electrons per molecule without requiring much energy.

Methods: To make the catalyst, researchers at Brookhaven National Laboratory in New York deposited tiny clusters of platinum and rhodium on tin oxide nanoparticles. Rhodium had been shown to break bonds between carbon atoms, but only at high temperatures—200 to 300 °C. Combining the rhodium and platinum with tin oxide allowed it to break these bonds at room temperature, making the catalyst more practical for portable fuel cells.

Next steps: The catalyst will be incorporated into fuel cells to determine whether the current produced can be increased from the 7.5 milliamps per square centimeter seen in initial tests to the hundreds of milliamps needed for most applications. TR

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www.iirusa.com/feiusa

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Atlanta, GA
http://convention.bio.org/

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May 20, 2009
Cambridge, MA
www.mitcio.com

Santa Barbara Summit on Energy Efficiency
May 20-21, 2009
Santa Barbara, CA
iee.ucsb.edu/sbsee

6th Annual MITX Technology Awards
June 16, 2009
Boston, MA
www.mitxawards.org/technology

EmTech@ MIT 2009
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Cambridge, MA
www.technologyreview.com/emtech

The Webs We Weave

LIE DETECTION HAS NEVER BEEN STRAIGHTFORWARD

By MATT MAHONEY

Methods for detecting lies have been around for as long as people have been telling them. There is something comforting in the notion that even the most skilled liar will unconsciously betray himself by some subtle cue—a reddening of the ears, a fidgeting of the hands, an uncontrollable shift of the eyes. But attempts to turn the art of lie detection into a science have always been controversial.

Although an automated version of psychologist Paul Ekman's system for analyzing facial microexpressions to detect deceit may soon be deployed in counterterrorism settings *(see "Telling," p. 78)*, and at least two companies are now marketing what they claim is a superior lie detection test based on functional magnetic resonance imaging (fMRI), the polygraph remains the best-known and most widely used lie detector nearly a hundred years after its invention. The polygraph is based on the principle that lying causes a physiological response in the teller that can be reliably measured by a machine and interpreted by a trained technician. In January 1981, a *TR* report on their then-prevalent use by employers described a typical examination:

The device typically monitors changes in breathing, blood pressure, pulse rate, perspiration, and electrical conductivity of the skin as the subject is asked a succession of questions by the polygraph operator.

The first questions, called "control questions," are designed to elicit a deceptive statement from the subject and hence yield an example of a deceptive response. ...Next, the polygraph operator poses questions relevant to the reason for the examination. ... The subject is generally considered to be lying when the observed responses to relevant questions are similar to the subject's reactions to control questions. The subject is deemed truthful when the responses to relevant questions are of lesser magnitude than those to control question, and when the pattern of reaction resembles truthful responses to irrelevant questions.

Questions about the validity of the polygraph have dogged it since its introduction, yet the device quickly gained popularity in the United States. Although a 1923 Supreme Court decision generally barred the use of polygraph results as evidence in court, the technology was widely used by both police and private investigators. Its use in the workplace was the most controversial application.

In recent years, the American public has expressed growing concern over the use of the polygraph, or "lie detector," for the selection and management of workers in industry and government. ...

The polygraph has become attractive to private industry because it is fast and cheap. ... Employers use the polygraph primarily to curb employee theft. ... Polygraphs are also used to verify employment applications and to assess periodically employee honesty, loyalty, and adherence to company policy.

Criticism of its reliability as a screening tool, combined with official outrage over President Ronald Reagan's attempt to plug leaks of classified information through polygraph examinations of all civil servants with security clearances, led

NERVOUS, PAL? A man in Greensboro, NC, being given a polygraph test in 1962

JACK MOEBES/CORBIS

Congress to pass the Employee Polygraph Protection Act of 1988, which prohibits private companies from requiring employees to submit to the test. Government employees at the federal, state, and local level are exempt from the act, however, as are contractors in security-sensitive positions; the number of federal polygraph programs has been on the rise in recent years. Critics argue that expanding the use of polygraphs in counterintelligence is especially dangerous, because the test can be beaten. Aldrich Ames, for example, passed multiple polygraph tests while spying for the Soviet Union in the 1980s and '90s.

But even assuming that a lie detector were perfectly accurate, its use would raise profound ethical questions. As the *TR* report concluded:

The use of a machine to "detect" lies is, arguably, inappropriate and impractical. More seriously, it violates our society's cherished ideals of individual privacy and civil liberties. As former Senator Sam Ervin opined in 1974, "If the right to privacy means anything at all in our society, it means that people are entitled to have thoughts, hopes, desires, and dreams beyond the grasping reach of a bureaucrat, an employer, or an electronic technician." TR

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